THE DEVELOPMENT OF A MICROCOMPUTER BASED REGISTER FOR THE STUDY AND MONITORING OF CROHN'S DISEASE IN TAYSIDE; ITS WIDER IMPLICATIONS AND APPLICATIONS.

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CONTENTS

SUMMARY

The development and potential value of a Crohn's disease Register is described. This thesis establishes that this can be accomplished using a microcomputer system. The wider clinical implications of the microcomputer development are also described.

The introduction overviews the present knowledge of Crohn's disease, examines the value and potential pitfalls associated with the establishment of a Register and investigates the background to the development of computing in the medical field.

For clarity the Register's development has been conveniently divided into medical and computing aspects. Much of the early work centred round the content of the Register's database and on defining the diagnostic criteria required for entry to the Register. A pilot scheme was introduced to evaluate the method of case ascertainment prior to full retrospective data collection. A description of the computer system, its philosophy and its facilities has also been given highlighting aspects of particular clinical relevance.

The computer system's data enquiry and analysis facilities were then used to investigate epidemiological aspects of the disease, overview the efficacy of investigative techniques and monitor methods of treatment. The resultant findings are intended not only to evaluate the medical content of the Register but also demonstrate the potential of the computers facilities both in this phase and for future prospective data collection and enquiry.

In discussion the more significant aspects of the Register's development and retrospective data collection are highlighted and the practicalities of prospective implementation considered. Finally the computer system is discussed in its wider context and its value demonstrated by the growing variety of clinical applications which have used

the system to help with medical audit, medical research and more recently patient management.

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DECLARATION

I declare that I am the author of this thesis, that the work of this thesis is a record of the work done by myself except where acknowledged, and that this thesis has not previously been submitted or accepted for a higher degree.

Signed

Michael Walker

CHAPTER 1

INTRODUCTION

1.1 CROHN'S DISEASE

The recognition of the existence of Crohn's disease is relatively recent. This can probably be explained by the lack of both autopsy and abdominal surgery in the eighteenth and early nineteenth centuries. However, careful re-examination of old case histories, such as the one described by G B Morgagni of Forli in 1769, may well represent early cases of Crohn's disease. In 1813 Coombe and Saunders reported a case of a man to The Royal College of Physicians of London who "had been for many years troubled with flatulency and complaints of the bowels". He later developed colicky abdominal pain several hours after meals and subsequently intestinal obstruction. At autopsy there were skip areas in the colon and they described ... "the lower part of the ileum, as far as the colon, was contracted for the space of three feet to the size of a turkey quill". A description which may well represent the first narration of a case of Crohn's disease. Several others including Abercrombie (1828) and Bristowe (1853) subsequently described findings at autopsy which were similarly suggestive of those of classical Crohn's disease.

Dalziel in 1913 (Dalziel 1913) described a series of nine cases on whom he had operated in Glasgow and whom he described as suffering from a new condition of 'chronic interstitial enteritis and not tuberculosis'. Of the nine operated upon four had disease in the small bowel, two disease in colon and small bowel and the rest disease in the colon alone. Nonetheless it was Crohn (1932) and his colleagues that attracted the attention of their fellow physicians when on May 13th 1932 they reported 14 cases of 'terminal ileitis' at a meeting in New Orleans. Since then and perhaps inappropriately Crohn et al have been attributed with the first true description of the disease.

Although the condition was initially described as a 'regional enteritis' it is clear from the early literature that cases of segmental colitis had been recognised in the 1930's (Dalziel 1932 and Hurst 1935). Wells (1952) appears to be the first to describe segmental colitis as a true colonic form of Crohn's disease, the pathology of which was confirmed by Lockhart-Mummery & Morson's classical paper in 1960 (Lockhart-

Mummery 1960). Since the initial description of regional enteritis many aspects of the disease have been extensively studied in an effort to obtain a better understanding of the disease process.

Much of the earlier work relates to the description of various features of the disease such as the typical and more unusual radiological (Marshak 1968, Stanley 1971, Goldberg 1979) and pathological (Lockhart-Mummery 1960, Cook 1973, Glass 1976) appearances. The introduction of flexible endoscopy in the early 1960's has resulted in similar descriptions of the features and the value of colonoscopy (Geboes 1975, Hogan 1980, Waye 1980).

A few have looked at the epidemiology of the disease and established evidence of varying trends in incidence and prevalence within countries (Kyle 1971, Maybury 1979, Ritchie 1981). Others have reviewed and summarised the frequency of disease across continents (Kyle 1972, Maybury 1984). This has not been an easy task. Firstly, the disease is not common and secondly, centres with a particular interest in the disease tend to attract cases often referred because of some difficult or unusual problem; thus a biased and ill-defined population is produced making valid epidemiological study impossible.

Others have looked at specific groups of patients, for instance the elderly (Carr 1982, Fabricus 1985) or those with perianal disease (Morson 1959, Fielding 1972, Buchmann 1980) because they present with particular problems, or in whom the disease process displays a distinctive pathogenesis.

Over recent years some large multicentre trials (National Co-operative Crohn's disease study (NCCDS) 1978 & Malchow 1984) have been set up in an attempt to rationalise the medical management of the Crohn's patient. However, many smaller therapeutic trials have also been undertaken in an effort to prove the efficacy of various medical regimes (O'Morain 1984, Jakobovits 1984, Schaffer 1984). Some have shown improvement in certain areas of the disease for instance symptoms - elemental diets

(Axelson 1977 and Goode 1976), total parenteral nutrition (Elson 1980) and in acute exacerbation of the disease where prednisone given over 4 months (Summers 1979) have been found to be effective in alleviating symptoms. Others have found that although steroids help in acute disease there is no evidence that they either prevent relapse of quiescent disease or recurrence after surgery (Bergman 1976, Smith 1978, Summers 1979). Similarly, although sulphasalazine has been shown to be effective in ileocolic-colic disease (Summers 1979, Van Hees 1981) it fared no better than placebo in ileal disease (Summers 1979) nor did it help prevent relapse or recurrence after resection (Lennard-Jones 1977, Wenckert 1978). The value of immunosuppressive drugs such as azothiaprine and 6-mercaptopurine either on their own or in combination with steroids or sulphasalazine remains unproven although there is some evidence that these agents may help patients with chronic active disease for whom it is difficult to withdraw steroids (Willoughby 1971, Present 1980). More recent studies have shown that methyl prednisolone is the most effective drug for active and inactive disease both in the small and large bowel - the European Co-operative Crohn's Disease study (ECCDS) (Malchow 1984) - and that metronidazole is helpful in colonic and perianal disease (Ursing 1975, Brandt 1982). Although cyclosporin has been shown to be of benefit in some case reports (Allison 1984, Bianchi 1984) further trials are required before the true efficacy of the drug can be evaluated.

Following the early descriptions of the disease in the 1930's and 1940's surgical resection was considered a curative procedure. Long term follow-up for as many as 15 years however established that recurrence rates reaching 80% (Ward 1954) occurred after multiple resection while Garlock (1954) reported a mortality rate of 16.4% following bowel resection. This led to an increasing use of by-pass procedures which reduced not only mortality but appeared to reduce the rate of recurrence. By the mid 60's the pendulum had again swung back in favour of resection prompted by reports from Schofield (1965) and Atwell (1965). In recent years, although stricturoplasty has been

tried, resection has remained the preferred method of operative treatment despite the fact that no fully randomised trial has been carried out to investigate the efficacy of resection, exclusion by-pass or by-pass in continuity.

Despite this work many clinicians managing patients with the disease would still agree that both medical and surgical treatment remains difficult and is often influenced by personal experience rather than by sound scientifically based policy.

Much of the reason for what might be considered an unscientific approach to the management of the disease has been attributed to the lack of knowledge available regarding its aetiology.

Several avenues have been explored in an effort to identify possible aetiological factors. Many attempts have been made to implicate transmissible infective agents (Beeken 1980), some have identified viral agents (Farmer 1973, Stickland 1979) while others have found bacterial and cell wall deficient organisms (Beekin 1973 and Belsheim 1980). The presence of granulomatous lesions, particular clinical manifestations, such as biliary and skin manifestations, and the fact that anti-inflammatory and immunosuppressive agents are used in treatment has resulted in the immune system being fully investigated (Jewell 1973, Mcpherson 1976, Mee 1979, Pugh 1979). Nonetheless the exact nature of the primary or secondary involvement of these immune mechanisms remains unclear. Dietary influences, in particular a high intake of refined sugar (Maybury 1978, 1980) and genetic factors (Kisner 1973, Lewkonia 1976) have both been implicated as other possible aetiological factors. Their true involvement however, still requires further investigation and clarification.

Despite exhaustive studies of individual factors none seems to have emerged as a single primary precipitant of the disease process. It is likely therefore that the aetiology is multifactorial in origin and that a greater understanding of their relationships may well be required before a more reasoned and scientific approach can be taken in formulating treatment regimes.

Overall, the extensive and valuable study of varying aspects of the disease has to date produced findings and conclusions which have in the main only shown how little is actually known about its pathogenesis. Indeed one could arguably suggest that much of this work has only highlighted the complexity of the disease rather than provide answers to the initial enquiry. This plus ambiguities in the definition of Crohn's disease and Ulcerative Colitis has prompted some to take a further look at what constitutes a diagnosis of Crohn's disease (Myren 1979). One approach to these types of question is to collect and examine epidemiological data (Maybury 1984).

Careful review has shown that despite much interest in the disease only a small number of sound epidemiological surveys of the disease have been reported (Brahme 1975, Miller 1974, Kyle 1979, Hellers 1979) and have often not been comparable. Reliable, up todate and consistent information on the epidemiology of the disease is therefore not freely available. Even in Britain despite its comparatively high standards of medical care and health service audit the incidence is subject to debate. Indeed it is not even clear whether the incidence is increasing (Fee 1985), stable (Maybury 1983) or decreasing (Kyle 1980) or whether the trends truly differ from area to area. Although this variation in incidence could result from data which is not comparable, for instance the use of different diagnostic criteria, or inaccurate data collection either in case capture or in determining the at risk population it is clear that further comparable studies are required to determine if there are real differences in incidence in different parts of the country. A major element in the development of comparable studies hinges on a uniform and generally accepted definition of what constitutes a case of the disease.

This thesis describes the establishment of a system for the collection and analysis of a basic epidemiological data set for Crohn's disease. The system has established the extent of the condition, provided an overview and facilitated audit of the

disease in Tayside. Furthermore it presents an opportunity to explore the pathogenesis of the disease and to develop a mechanism with the potential to help in patient management.

It was clear from examining available epidemiological information that several important considerations had to be taken into account before an appropriate data set could be drawn up.

There are various definitions of Crohn's disease (Lennard-Jones 1976, Myren 1979) which probably accounts for the 16 eponymous terms which Fielding (1972) found on review of the literature. Most definitions include clinical, radiological and pathological features and only differ in minor respects while some take onset of symptoms as opposed to date of diagnosis as the disease start point. A set of diagnostic criteria therefore had to be defined clearly and efforts made to keep the criteria comparable with other study groups. The criteria chosen for use in this Register are based on the internationally agreed system drawn up by the OMGE group (Myren 1979). The scoring system will be fully described in a subsequent chapter of this thesis.

Completeness and accuracy of data collection within a well defined population was mandatory and much thought was given to the methods employed in case ascertainment and confirmation of disease.

The approach eventually chosen was to collect and collate a basic epidemiological data set linking more detailed information on specific aspects of the condition. Crohn's disease as a chronic and sometimes debilitating disease carries a high morbidity with a lower though not insignificant mortality. The natural history of the disease therefore lends itself to an on-going data collection process. To match the chronic nature of the disease a structured data set was created to permit the ongoing collection of this information thereby enabling a patient's progress to be monitored over a period of years. A dynamic and changing picture of Crohn's disease in the Tayside population would then evolve over a period of years. The collection of data for

epidemiological analysis should be a by-product of the clinical monitoring and management process and would therefore benefit in quality and completeness from this approach without duplication of effort and resources.

Although many difficulties exist in the development of disease registers of this nature it was felt that this format remained the most appropriate.

1.2 REGISTERS

The Oxford Dictionary defines a Register as 'A book in which regular entry is made of details of any kind sufficiently important to be exactly recorded'. The verb is defined as 'the setting down of facts in writing or to record information in a precise manner'.

The 'Domesday Book' prepared in 1086 to ascertain the value and extent of land managed by the King and his sub-tenants was probably one of the first and most complete Registers ever prepared. It demonstrates many of the important aspects of any Register as it contained only the vital parts of the total data initially collected, information which was then used to good effect by the treasury in its daily administration.

Through the centuries the concept of Registers continued to develop as their potential value was realised. In 1753 efforts to introduce the 'Census Bill' provoked much resistance and resentment because of the threat to 'English liberty' and it was not until 1800 that the first census act was passed which eventually led to the foundation of the General Register office in 1836. This was the forerunner of the present day Registrar Offices of England and Wales, and the separate Scottish Office which continue to collect morbidity statistics on the population as a whole. These registers remain some of the most complete because of the importance of much of the information collected; the birth and death of an individual are unlikely to be overlooked.

The blind Register, one of the earliest and probably the first disease specific Register, began its evolutionary development in 1911 (Saunders 1973) and continues to provide valuable and accurate monitoring of the blind population.

Although formal British Cancer Registration began in 1930 (Stocks 1950) the first efforts to collect information on malignant tumours probably began in 1728 (Clemensen 1965) but were hindered by the scarcity of available definitive diagnostic techniques. Other notable developments were the advent of the Scottish Morbidity Returns (e.g SMR1, SMR11, SMR2) set up in Scotland in 1961, the in-patient returns for

England and Wales which audit hospital admissions for the whole country, and more recently ischaemic heart disease registers such as the United Kingdom Cardiac Register (English 1984) many of which were formed on the basis of the World Health Organisation reports of 1969-70 (WHO 1969, 1970).

There are many types of medically related registers. Weddell (1973) in a review of registers classified these into seven types:

a. Registers to help in preventive medicine for example screening and immunisation programmes.

b. Disease specific - which are common and include those for ischaemic heart disease or malignant disease.

c. For use in treatment and patient management such as the Scottish Automated Follow-Up Register (SAFUR) set up in 1967 to automate follow-up of thyroid disease in Scotland (Hedley 1970).

d. Aid in after care of the handicapped, disabled or other compromised groups.

e. To monitor at risk populations such as the deaf, mentally retarded or chronic sick.

f. To take note of such scarce resources and skills as rare blood types or transplantation programmes.

g. Prospective studies which are many and varied, and were described as difficult to run and often costly.

h. Specific information registers such as the poisons bureau and registers of congenital defects.

This demonstrates the many topics that can be helped by a register and the varied ways that this form of data collection can be put to use.

Registers are however recognised to be notoriously difficult not only to implement but also to operate and manage successfully. This is mainly because they can consume a large amount of resources, especially time, both in obtaining complete case

ascertainment at the time of implementation and subsequently maintaining the register in up to date and accurate fashion. It is therefore extremely important that firm objectives are laid down regarding the expectations and functions of any proposed register.

The successful development of any register is dependant on three important factors:

a) Completeness

b) Accuracy

c) Usefulness.

a) Completeness

Completeness of data collection is vital if a valid register is to be developed. Few registers ever achieve this however, and those that do more often than not contain information which is unlikely to be overlooked for example mortality data. Doll (1970) reporting on cancer incidence in five continents found that all the cancer Registers were incomplete - estimated shortfall varying from 2.5% to 15% - and pointed out that if registration is to be considered to be complete it must involve collection of data from a number of sources and must provide a means of cross checking to prevent duplication of entries.

Also important is the extent to which cases are reported, a fact emphasised by Crooks (1970) who commented that the United Kingdom blind Register was nearly complete - estimated 3% not registered - because of the efforts of well co-ordinated voluntary bodies and because there were financial benefits accruing to those registered.

Interestingly Chiazze (1966) comparing the completeness of registers against specifically designed surveys of patients suffering from cancer found that surveys tend to overestimate numbers while registers underestimate because of incomplete reporting.

b) Accuracy

The validity and the value of information contained on a register is dependant upon the quality of data capture. Cross checking of data from a number of sources is essential to ensure accuracy and to avoid duplication of entries - for example a clinical diagnosis should be confirmed by a histological diagnosis or post mortem examination. Furthermore the quality of medical data and its subsequent collection relates to the accuracy of clinical diagnosis, a factor which is dependant on the provision, access and standard of medical services available to the population.

c) Usefulness

The objective of a register should be well defined (Weddell 1973) and should provide information on such topics as the prevention and treatment of disease, provision of after care, the evaluation and planning of services and monitoring the changing patterns of disease. The specified objectives of a study therefore require to be examined regularly and if the functioning register fails to meet the objectives changes should be implemented or closure of the register considered. Importantly however, patient record and recall systems should be designed to enable them to respond to changing circumstances. The availability of such systems can itself bring changes in methods of care, and treatment regimes.

The introduction of computer technology to data processing has enabled information to be stored and analysed with minimal difficulty. With the opportunity to collect large volumes of data the investigator must resist the temptation to collect quantity at the expense of quality. Just as in retrospective data collection where each item collected should serve a purpose the emphasis should be placed on the collection of data vital to the fulfilment of the stipulated objectives of the register.

The potential value of a dynamic medical information system able to respond to changing circumstances needs careful consideration before implementation and regular

review in order to avoid possible closure from failure to meet it's objectives. Furthermore the role of any new system should be examined in relation to existing methods of clinical practice. Systems demanding radical changes in the behaviour of clinicians particularly in respect of entry of data into computer systems run considerable risk of failure. It is therefore essential that any such system should be developed primarily to increase the efficiency or effectiveness of the service provided while the audit and research should be considered an essential and invaluable by-product of the exercise.

The use of computers and their application to medical registers is reviewed in the next chapter.

1.3 COMPUTERS IN MEDICINE

The use of computers in medical practice is now firmly established yet it is only 20 years since the first attempts to produce a system providing a full case record on a computer. One of the first was the SWITCH system (Kennedy 1968) which used a record tape to encode the data onto the computer and which was designed in an effort to provide a database from which data retrieval and audit could be achieved. Further systems followed such as COSTAR - a computerised ambulatory record system implemented in the Massachussetts General Hospital - each based on a very large, complex, and by today's standards, crude computer. The development in the 1970's of increasingly complex integrated circuits led to the production of the microprocessor and high density semiconductor memories. Hardware advanced rapidly following this development and led to a marked reduction in size of each machine and a similar increase in power, speed and sophistication.

Unfortunately the development of health care orientated systems appears to have progressed along two separate paths. One has been concerned mainly with the administration side, where large capital sums have been invested in 'mainframe' systems to perform administrative tasks - for instance for the pay-roll, financial management or stock control - and are often divorced from mainstream clinical practice. Indeed figures for 1980 show that only 25% of health service computer related revenue expenditure in both Scotland and England is directed at computer resources for patient management or direct medical application (Herbert 1982). These systems have usually had priority over the smaller clinically orientated projects which have commonly been set up by enthusiastic clinicians with the help of donations from the pharmaceutical industry or friendly societies. This historical quirk has resulted in the creation of two distinct types of health care systems which often contain overlapping data sets. The co-ordinated development and integration of these different systems should prevent a duplication of input of such

data as patient identifying information. The diverse origins of these systems makes the task of bringing the different types together extremely difficult. Only recently have groups been set up at local and national level to oversee and co-ordinate computer related activities. Unfortunately it will be some time before systems can work together as components of an overall medical information network.

One thing is clear however, the continued development of clinically orientated health care computer systems is assured with an ever growing list of general and dedicated applications appearing in the literature. These systems have their origins in one or a combination of simple audit (for example age/sex register), management administration (for example laboratory, patient administration and recall systems) and research functions.

Many of the early systems were used to perform a simple audit, for example SWITCH (Kennedy 1968) and inflammatory bowel disease registration (Rogers 1971), and were used as simple data collection mechanisms which could then be audited thereby providing data for research. Others were developed to test the value of computerisation against the existing manual system - hypertensives (Bulpitt 1976). Later it was felt that systems of computerised records may be of potential value in aiding patient management, particularly in the situation where patients required essential periodic follow-up.

SAFUR set up in 1967 (Hedley 1970, Hedley 1970a) encompassing centres throughout the North East of Scotland to aid in follow-up of patients with thyroid disease was one of the first of these patient management orientated systems in this country. Other conditions lending themselves to this form of structured patient record follow-up were tackled, with hypertensive (Petrie 1985), diabetic (Watkins 1980, Jones 1983) and psychiatric (Ancill 1985) groups being at the forefront of this development.

Patient orientated primary care systems have also been developed and are being increasingly used in general practice (GPASS, VAMP, AIBES). Indeed some have even been built around an automatic method of repeat prescribing for example GPASS.

However systems are now being developed into true integrated packages designed to help manage a combination of practice requirements with modules for registration, repeat prescribing and accounting.

Much of the development work on clinically orientated patient record systems has however centred round the development of computer assisted diabetic Register and Information systems (Levy 1964, Watkins 1980, Jones 1983). These systems have been implemented firstly in an effort to improve the standard and accuracy of medical data collection over the traditional, often illegible, case record and secondly to use that information for service planning and research to increase the standard of patient care. Jones (1983) described several necessary requirements of such a diabetic system if it were to meet the objectives of a register. The system should hold basic identifying patient data along with social, demographic, clinical and therapeutic information which should all be linked and available for use by other clinicians. The recent introduction of the Korner data sets in England and Wales following the reports of the Korner steering group on Health Service Information (Knox 1987) has more clearly defined the basic data requirements of any data collection system and indeed overlaps the ideas previously described by Jones. The use of the standard Korner data sets should now be considered as mandatory. There should be a 'fail-safe' mechanism to prevent patients being lost to follow-up while the increased use of automatic monitoring for certain groups of at risk patients would require a reliable method of communication between hospital doctor, patient and general practitioner. Hedley (1985) suggests that the correct implementation of this type of system will encourage new methods of care firstly because some labour intensive tasks can readily be performed by the computer for instance the creation of at risk groups with certain clinical characteristics requiring closer monitoring and secondly by measuring and assessing the efficacy of different follow-up regimes. The recent introduction of diabetic shared care schemes is one example of this type of development. These ideas are receiving further support, for instance the recent Anticipatory Care Team

conference (ACT 1987) which highlighted the value of the 'Anticipatory Care Team' strategy in cardiovascular risk screening.

There have however been some major problems associated with the development and introduction of these computerised systems:-

a) Difficulties in changing the clinicians working practice.

b) Medicine is an inexact science and much information therefore requires careful coding if accuracy and consistency of the data collected is to be maintained.

c) Objectives within a particular application are often poorly defined.

d) Poor links between manual handwritten records and the computer database. The database will only be as good as the information it has been asked to store. Two major points arise here:

1. If little thought is involved in deciding what questions the users want to answer from the database then inappropriate data may be collected and vital data may be omitted from the database.

2. Data input is always a weak link in any computer system therefore some form of validity checking is important to reduce this type of operator error.

e) Difficulties of physical access to mini or mainframe computers for which there is an increasing demand.

f) High costs of maintenance and purchase of hardware and even higher costs involved in software development - often not recognised.

g) Problems of portability of data between different types of hardware and operating systems. With the rapid development of hardware it is important that data can be moved from an old to a new system with minimal difficulty.

High volume sales of the rapidly developing Personal Computer (PC) in the business world has resulted in a significant reduction in cost of what are now powerful microcomputers. The cost of many are now well within the budget of hospital departments. This, coupled with recent government policy following the Korner reports (Korner 1985) suggesting a decentralisation of Health Service computer resources in the short term, with eventual inter-communication with the next generation of mainframe patient administration systems (PAS), has released funds enabling personal computers to be bought by many departments for word processing, data management, audit and research purposes.

Over the past few years there have been a growing number of reports in the medical literature relating to the use of this microcomputer technology for a growing number of medical applications. Many of these applications have been set up within the confines of a research or academic environment or by the enthusiastic amateur (Large 1985, Benveniste 1985, Sellu 1986 Adams 1986) often with minimal resources. On the other hand commercial enterprises having saturated the business end of the market have now turned to smaller less lucrative areas such as the medical market, and are now marketing a wide variety of often excellent systems, albeit at considerable cost.

Most area health authorities have had computing facilities for many years. However most are mainframe orientated and many of the staff have neither the experience nor the time to develop microcomputer systems. Although commercial software houses produce excellent general purpose database management systems these are aimed at the business user and have not proved to be so well suited to the clinical situation which often requires a combination of clinical management, audit, follow-up, research and analysis facilities.

The introduction of the much acclaimed but as yet not fully proven patient administration systems (PAS) will have a major impact in health care computing. The role of the microcomputer based sub-system within the PAS framework should be to

complement these larger mainframe systems, extending their benefit to the clinical level. This may well come about by using the microcomputer not only as a stand alone machine but also as an intelligent distal terminal existing in symbiosis with the patient administration systems.

Indeed it is the author's belief from this review that clinical audit at area level should be based on unit audit systems. These system would collect data relevant to that unit and produce as a byproduct information appropriate at area or district level. Subsets of this data could then be passed 'upward' to a higher level information system (for instance district level) which could subsequently pass a further more refined subset to area or national level. This would be possible because much of the clinical audit required at area level for resource planning and budget management is simply a byproduct of the patient management process.

The introduction of a computer system such as that proposed for the Register discussed in this thesis might therefore have some long term implications. A careful evaluation of both the hardware and software options was therefore imperative before development began.

CHAPTER 2

DEVELOPING THE REGISTER

2.1 OBJECTIVES

To achieve the proposed objectives of a disease register containing a computerised case record of each patient with Crohn's disease in Tayside with facilities to help increase the understanding of the disease it was necessary to break the development of the project into two major phases.

a) The generation of a suitable retrospective database containing information which would act as a foundation for the eventual prospective implementation of the register.

b) The development of a computer system on which to base the register. Facilities within the system would be required not only to log and recall data but also to permit data enquiry and analysis.

In this way the Register would not only contribute to the epidemiological study of the disease but also have the potential to help in patient management. Furthermore the database created would be a valuable research tool in its own right.

It was intended that the retrospective data collection, recording and subsequent analysis would act as a pilot study enabling a full assessment of the value and feasibility of the proposed register. Developing the register in this manner would also prove a sound test for the computer programmes. Furthermore if the Register were to be implemented prospectively the experience gained from the retrospective data collection could be used to make improvements to the prospective database design.

The development of the Register was therefore divided into

a) The Medical aspects

b) The Computing aspects

2.2 THE MEDICAL ASPECTS

The proposed aims of the Register were

a) to develop a mechanism which would provide an overall picture of Crohn's disease in Tayside

b) to create a tool to help in patient management

c) to supply information on which further research might be based.

In order to achieve these aims a large volume of data would require to be collected.

To help achieve these objectives and thereafter to assess the value of the Register the generation of the database was divided into several convenient sections:-

1. defining the Register's diagnostic criteria
2. structuring the database
3. collecting data retrospectively

2.2.1 Diagnostic criteria

The validity of the register would depend on the accuracy of the data it contained. The first step therefore was to decide on the criteria to be used by the Register to determine what would constitute a diagnosis of Crohn's disease.

The separation of Crohn's disease and Ulcerative Colitis can be a difficult task and is arguably one of the commonest diagnostic problems in gastroenterology. Up to 20% of individuals thought to have Inflammatory Bowel Disease have been described as 'unclassifiable' (Morson 1971); a finding which can be explained by individuals who have for instance clinical features of Crohn's but radiographic evidence suggesting Ulcerative Colitis. Most groups develop their own working diagnostic criteria which takes

into account the recognised clinical, pathological, radiological and endoscopic features of the disease (Kyle 1971, Lennard-Jones 1976, Lee 1981). Each places a different weighting on individual criteria depending on their impression of the importance of that feature. Recent work by the Organisation Mondiale de Gastroenterologie (OMGE) has resulted in the development of a scoring system for separating Crohn's disease from Ulcerative Colitis (Myren 1979). This system is based on the probabilities of an individual with a specific feature or group of features having either Crohn's disease or Ulcerative Colitis. Indeed this group has suggested this scheme be adopted as a 'gold standard' which others might follow in order to obtain a degree of uniformity between workers and to permit direct comparison between groups. This method had a commendable predictive value of 93%, however it appeared to have one major flaw - it assumed that all those submitted to the scoring system were suffering from Inflammatory Bowel Disease. This diagnosis is of similar importance however, and on occasion is equally difficult to make.

In order to clarify this important distinction within the Register Inflammatory Bowel Disease was defined as that patient group who were considered to have Crohn's or Ulcerative Colitis. This may seem pedantic however it provides exclusion criteria for those patients with for instance radiation proctitis and endometriosis who if submitted to the OMGE scoring system may be classified as Crohn's or Ulcerative Colitis and hence entered into the Register.

It was therefore decided to base the Register's diagnostic criteria on two stage serial testing, firstly,

a) Is this a true case of Inflammatory Bowel Disease or some other Non-Specific Colitis?

and secondly,

b) Is this Crohn's disease or Ulcerative Colitis?

It was hoped that this would maximise specificity and positive predictive value and although perhaps lowering the sensitivity of the diagnostic method it should ensure that those noted to have positive tests did have Crohn's disease.

This serial testing would firstly produce a group considered to have Inflammatory Bowel Disease who would then be further subdivided into those with Crohn's disease and Ulcerative Colitis; the Crohn's group would then be admitted to the Register.

The scoring system devised takes into account the individual's clinical, radiological, endoscopic and pathological findings. Patients were considered to have Inflammatory Bowel Disease if they had symptoms of the disease and had demonstrated positive evidence of Inflammatory Bowel Disease in at least half of all performed relevant investigations.

The developed scoring system attempts to take into account the relative importance of the various traditional techniques used in the diagnosis of Crohn's disease or Ulcerative Colitis. For instance greater weighting has been given to the pathological and radiological findings as compared to endoscopic findings. The system is described below.

A. Symptoms:-

Score one point for each bowel related symptom.

B. Endoscopy:-

Score 0 = no evidence Inflammatory Bowel Disease (IBD)

1 = some evidence IBD

2 = good evidence IBD

C. Radiology:-

Score
0 = no evidence IBD
2 = some evidence IBD
4 = good evidence IBD

D. Pathology:-

Score
0 = no evidence IBD
1 = minimal evidence IBD
3 = good evidence IBD
5 = diagnostic of Crohn's / Ulcerative Colitis

A total patient score of 6 or above with half of all Crohn's related investigations positive was arbitrarily considered to represent a case of Inflammatory Bowel Disease (IBD) as opposed to an indeterminate or Non-Specific Colitis.

The scoring system was tested for accuracy by checking groups of patients who were known to have either Crohn's, Ulcerative Colitis or Non Specific Colitis. The predictive values using this scoring method were 98% and 100% for those who were thought to have Crohn's disease and Ulcerative Colitis respectively and showed a specificity of 100% for those thought not to have Inflammatory Bowel Disease (ie had Non-Specific Colitis) (fig 2.1). Even though the test populations are small it is clear that this simple test is a good indicator of Inflammatory Bowel disease. These findings will be discussed more fully in a later section of this thesis (Chap 5).

If a patient met the criteria for Inflammatory Bowel Disease then the well recognised OMGE group's score scheme was applied to separate those with Crohn's disease from those with Ulcerative Colitis. A separate diagnostic proforma was designed so that a potential Crohn's patient could readily be screened using this technique (appendix 1a,b,c).

Test	Crohn's disease		Predictive value
	yes	no	
scoring +	42	1	98%
system -	5	2	

	Ulcerative Colitis		
	yes	no	
scoring +	42	0	100%
system -	1	4	

	Non-Specific Colitis		Specificity
	yes	no	
scoring +	3	0	100%
system -	3	42	

Accuracy of diagnosis for Inflammatory Bowel Disease

Figure 2.1

2.2.2 Content of the database

The appropriateness of the structure and content of the database was vital if the data was to answer the questions posed by the users of the register. This indeed could be considered the most important part of the Register's development. It must be borne in mind that any data management and analysis system can only be considered as good as the data it contains. The content of the database was conveniently divided into sections each containing related data.

A. Epidemiological and General information

This section would contain basic information relating to a patient's history and examination (appendix 2) and provide all the data required to produce an epidemiological picture of the disease.

Basic identifiers such as name and address along with the patient's General Practitioner identifiers would also be collected. This information would be crucial if the Register was to function as a management tool where personalised letters, appointments and reports could be produced as an integral part of the system.

B. Investigations

To create a more detailed picture of the disease and to monitor the natural history of an individual's disease it was decided to keep a careful record of all the commonly performed investigations. This would enable an accurate audit to be performed and enable some measurement of the value of each investigation to be made at different stages of the disease. Data was collected under four headings.

a) Pathology - To include both macroscopic and histological information on specimens submitted as a consequence of or related to Crohn's disease.

b) Radiology - Information on Crohn's related radiological investigations plus their findings and diagnosis.

c) Haematology/Biochemical data - Parameters thought to be of most value would be gathered in a sequential fashion.

d) Endoscopic information - All endoscopic procedures and their findings would be logged in the Register.

Dates would be kept for each investigative sub-section to enable monitoring and comparison of repeat investigations against time. Appendix 3 shows the detailed investigation data collection form. Facilities within the computer system would be developed to allow the data to be collected in a time related fashion thus creating a chronological record of investigations for each individual on the register.

C. Treatment

Information relating to both medical and surgical treatment was also included in a format which would permit regular update and recall. Data would be collected on drug therapies and dietary manoeuvres, while surgical data would include indications for and type of operation performed. Each treatment would have an associated date enabling comparisons to be made with for instance date of diagnosis and dates of recurrence. It was proposed that the prospective data collection would link treatment information to a disease activity score enabling indirect measurement of the efficacy of treatment and patients well-being over a period of time. Provision was therefore made within the treatment file for collection of data relating to disease activity. Many systems have been devised in order to measure the disease activity (Harvey 1980, Elliot 1980) of patients with Crohn's disease. Some use objective measurements as an indicator of activity (Van-Hees 1980) while others rely on more subjective assessment (Best 1976). The activity index chosen is the well described Crohn's Disease Activity

Index originally described by Best (1976). It would however be impossible to collect disease activity in the initial retrospective data collection.

The data proforma used to collect treatment information is shown in appendix 4.

D. Morbidity

Crohn's disease is a chronic disorder with little mortality but considerable morbidity. Measurement of patient morbidity would give some idea of the distress and inconvenience caused by symptoms over a period of time. It was therefore intended that morbidity data should be collected periodically for all or groups of patients on the Register. The data files were developed to include certain information relating to morbidity (appendix 4).

Once decisions had been made as to the content of each section of the database the information was expanded into a questionnaire which was designed for use with a computer system. This resulted in the production of a proforma with 175 data fields which contained a total of 507 data points. The data was conveniently divided into four major sections -

1. diagnostic information
2. general information
3. investigations
4. treatment, disease activity and morbidity.

This would facilitate the generation of a database containing four data files.

2.2.3 Retrospective Data Collection

The retrospective collection involved several important steps:-

A) defining the population on which the Register was to be based

B) determining the Crohn's cohort from the defined population and checking for accuracy of diagnosis

C) collecting the appropriate information on questionnaire ready to enter into the computerised register

A) Defining the population

One measure of the validity of a register is its completeness therefore the first task was to identify the Crohn's population within a defined area.

Tayside Region is a good area in which to undertake epidemiological research because of the static nature of the population. Census figures for the past century show that there has been very little change in the population during this time.

Census	population	period change	%
1891	394824		
1921	388433	-6391	1.6%
1951	396194	7761	1.9%
1961	397820	1626	0.6%
1971	397605	215	.05%
1981	391846	-4348	1.1%

Table 2.1 Change in Tayside Population

During the period 1891-1981 there has been no change in the regional boundaries while the largest swing of population between two ten year census points was in 1931 when there was an increase of 11,134 which represented an increase of 2.9% from the 1921 figure.

Comparing age/sex distribution over the period of study further demonstrates the static nature of the population.

	total population	Males		Females		M/F ratio
1961	397820	187378	(47.1%)	210442	(52.9%)	.471
1971	397605	189413	(47.6%)	208192	(52.4%)	.476
1981	391846	186267	(47.5%)	205579	(52.5%)	.475

Table 2.2 Change in Sex Distribution Population

The region covers a large area geographically and is divided into three health districts each served by a hospital group. Dundee district, the main centre of population, contains a teaching hospital group - Ninewells Hospital and Medical School, Dundee Royal Infirmary and Kings Cross Hospital. Perth & Kinross district is provided for by Perth Royal Infirmary while Angus district is served by Stracathro Hospital and Arbroath Infirmary. Several smaller cottage hospitals supplement the bed compliment within each district - each is run by General Practitioners although most also have out-patient clinics staffed by visiting Consultants.

Due to the distribution of population and position of hospitals within the Region it is unusual for General Practitioners to refer patients to hospitals outwith the area. Consultants wishing further specialist opinion on patients with Crohn's disease almost always refer to specialists within the teaching hospital group where there are several consultants with a particular interest in Inflammatory Bowel Disease. This situation is however complicated because some areas of neighbouring Fife region are close to Perth Royal Infirmary and others to the Dundee teaching group of hospitals. This results in some patients resident in Fife being referred to Tayside hospitals. Statistics confirm that Tayside health authority is a net 'importer' of patients from in particular Fife but also Grampian region. Calculation of the effective catchment population for General Surgery in Tayside for 1983 for example revealed a figure of 445,210 some 50,000 more than the official resident population. The inpatient cross

boundary flow for Crohn's disease and related disorders for patients in Tayside is shown in fig 2.3 confirming that few patients are "exported" to other areas. This study has shown that only 60% of those with a SMR1 diagnostic code of Crohn's will have the disease reducing this cross boundary flow still further. Furthermore, the figures relate to admission events some patients may therefore have several admissions. For technical reasons the Information Services Division, from whom the figures were obtained, were unable to provide figures for other than 1986.

	patients imported	patients exported
Crohn's disease	23	2
Idiopathic Colitis/ Other non-infected colitis	24	7

Table 2.3 Cross Boundary Flow in Tayside for Crohn's & related disorders for 1986

Despite the difficulties associated with collecting data from patients referred to a variety of hospitals it was decided that the Register should relate to all those Crohn's patients living in Tayside or being seen in the Tayside group of hospitals. Provision would be made in the database file structure to separate individuals into separate cohorts depending on their place of residence. In order to achieve this objective the postcode both at the time of diagnosis and the present time would be collected for each individual admitted to the Register. This would enable the Register to develop from a well defined population, thus meeting one prerequisite of any accurate epidemiological study, but would also provide as large a cohort as possible for non-epidemiological enquiry.

The population defined, it was then necessary to choose a time interval on which to base the retrospective data collection. Several factors required consideration :-

1) the period chosen should provide sufficient information to enable an accurate and valid picture of Crohn's disease to be built up within Tayside. Furthermore it should permit a comparison of trends following prospective data collection.

2) Scottish inpatient morbidity information, which includes diagnostic coding, has been collected since 1961. Over the years the format of collected data has however changed. Before 1968 the information collected related to hospital number, date of admission and discharge along with diagnostic coding. Tayside no longer has record of a full pre 1968 inpatient index to enable patient records to be identified and examined in those patients hospitalised with Crohn's disease before this time. Data retrieval on these patients is therefore all but impossible unless further admissions have taken place in the post 1968 period.

Since 1976 the Tayside Community Health Index (CHI) - initially developed as the Master Patient Index - has been computerised. This patient index contains inpatient disease codes based on the International Classification of Diseases (ICD), obtained from the SMR1 discharge form, thus making it relatively easy to obtain diagnostic information on all inpatients. Although the most recent outpatient contacts are held on this system no note is kept of outpatient disease coding. This presented a potential problem in defining the total Tayside Crohn's population. If individuals were diagnosed purely on outpatient visits then they would not be identified in a search of the CHI for those with a Crohn's diagnostic coding.

3) the International Classification of Disease (ICD) has changed twice over the years 1965-1975, with several other minor revisions, fortunately the coding structure for Crohn's disease has altered little over this period.

Taking these points into account it was decided to identify all patients in Tayside who were either diagnosed or were known to be suffering from Crohn's disease between 1968 and 1983. This would be achieved by obtaining information on disease codes from

i) Tayside Community Health Index

ii) Scottish Common Services Agency

iii) Tayside General Practitioners

B) Identifying and checking accuracy of population

Most agree that nearly all patients with Crohn's disease will be admitted to hospital at some point (Langman 1981, Langman 1983), indeed Kyle (1981) found that all patients in the Grampian series were admitted at some stage in their disease. The majority of patients should therefore be 'captured' by using the International Classification of Disease codes contained within the Scottish inpatient morbidity returns (SMR1) for the area under study. There are however possible pitfalls in using inpatient statistics alone for identifying and measuring the Crohn's population or any other disease population. Firstly, some patients may never be admitted to hospital although this is recognised to be uncommon in Crohn's disease. Secondly, some patients may have the disease for many years before hospital admission is required and in a few the diagnosis may only become apparent after hospital discharge and subsequent outpatient investigation. Thirdly, there may be inaccuracies in the coding itself. Fourthly, repeat admissions, lengthening of both out and inpatient waiting lists and improved medical treatment may appear to alter, at least on paper, the frequency and incidence of disease.

Langman (1983) suggested that inpatient statistics of Crohn's disease, unlike Ulcerative Colitis, give a reasonable index of the disease, however Smith from the Clydesdale series (Smith 1975) reported the inpatient statistics to be wholly inaccurate with a marked tendency to over diagnosis. In this series almost 50% of those labelled as sufferers of Crohn's disease following a hospital admission were incorrectly coded. A similar inaccuracy was also noted by Humphrey's (1975) in his series from Northern Ireland. The accuracy of the SMR1 ICD diagnostic coding will vary between health boards and may indeed vary between units depending on who completes the SMR1 form. Inaccuracies such as these would be eliminated by examining the case records of those deemed to have Crohn's disease by SMR1 returns, similarly patients with repeat admissions could be identified during this search. However this would give no measure of

the false negatives; those who had been incorrectly coded as Ulcerative Colitis or Non-Specific Colitis but who in fact had Crohn's disease.

Most series take the date of diagnosis as the basis for calculating incidence and prevalence rates. Using this data errors may arise from delays in reaching a diagnosis. Kyle in the Grampian series (Kyle 1971) eliminated this inaccuracy by using the onset of symptoms as the start point of the disease. It seemed that the best way of obviating this problem yet permitting comparison with other series was therefore to collect both date of symptom onset and date of diagnosis; this would also demonstrate any differences in calculated rates between the different methods.

Identification of the Crohn's population was conveniently divided into three stages.

1. The first step was to test the accuracy of the SMR1 diagnostic coding system for Ulcerative Colitis, Crohn's disease and Non Specific Colitis within Tayside. If the numbers of false negatives in the Crohn's group and false positives in the Ulcerative and Non-specific colitics were small then examining the case records of those with the Crohn's ICD code should prove a valid method of identifying all the false positives.

Computer print-outs were obtained from the Tayside Health Board inpatient statistics for the ICD codes of Ulcerative Colitis, Crohn's disease and Non- Specific Colitis for the year 1980-81.

The records of the first 50 Patients from each group were examined for diagnostic accuracy. All patients chosen were admitted to Dundee district hospitals, the years 1980-81 being chosen as this would provide a follow-up period of sufficient length for subsequent confirmation or otherwise of the original diagnosis.

The initial diagnosis was accurate in 90% of ulcerative colitics and 87.5%, of non-specific colitics but was inaccurate in 24% of those labelled as Crohn's disease after following each group for at least two years. Furthermore, of those given an incorrect diagnosis during the 1981 admission only 2% of those with an Ulcerative Colitis and 6%

of those with a Non-Specific Colitis coding were subsequently found to have Crohn's disease. These figures suggested that within Tayside the inpatient SMR1 returns were fairly accurate for those with Ulcerative Colitis and Non-Specific Colitis. Similarly of the false positives in these groups who turned out to have Crohn's disease after two years of follow-up,all eventually were found to have a Crohn's ICD coding following a subsequent admission. The results of this short study are more fully described in Chapter 4.

2. In view of these figures it was felt acceptable to base the initial case capture on inpatient Crohn's ICD coding particularly as so few individuals diagnosed initially as Ulcerative Colitis or Non-Specific Colitis had subsequently turned out to have Crohn's disease.

Print-outs were therefore obtained for all patients with Crohn's ICD coding for the years 1967-83. Information for years 1967-74 was obtained from the Scottish Common Services Agency while data for 1975-83 was obtained from the Tayside Health Board Community Health Index. The case records of all patients listed on the printouts were then obtained, examined and checked for diagnostic accuracy. If they met the register's diagnostic criteria they were then submitted to the general retrospective data collection.

3. It was felt that this procedure would capture all but a few Crohn's patients who had not had a hospital admission. To identify the remainder of the patients the ninety primary care practices in Tayside were mailed. The letters contained a list of patients belonging to each practitioner within the practice deemed to have Crohn's disease by the criteria laid down by the Register. General Practitioners were asked to add any other patients within their practice whom they considered to be suffering from Crohn's disease. The three practices with no apparent cases of Crohn's disease were also

mailed with a letter explaining the purpose of the study and asking the Practitioners to submit names of any patients within their practice whom they felt had Crohn's disease.

This particular method was chosen as it was thought that better practitioner compliance would result if reliable information was provided. All the additions were then checked using the recognised Register criteria, particular attention being paid to the date of symptom onset and diagnosis as individuals whose diagnosis was made after 31 Dec 1983 were excluded from the Register.

As many as 15% of patients wait up to two years for a diagnosis (Kyle 1977) to be made therefore the primary care mailing was not undertaken until September 85 in order that the names of those with symptoms and / or diagnosis prior to 1983, but no hospital admission until after 1983, might be obtained.

C) Retrospective collection of data

The case record of each potential Crohn's patient was identified and then carefully examined by the author and a Register diagnosis obtained. It is arguable that an independent assessor should also have validated the author's interpretation of the case record data and hence his 'diagnostic accuracy'. The conclusions of the OMGE study (Myren 1979) however, emphasise in particular the 'degree of congruence observed amongst participating clinicians in respect of diagnosis' which though achieved with structured proforma did not define the terminology used. With this in mind it was felt that because a similar proforma was used in this study further observer validation was not necessary.

This involved identifying those with IBD through the developed scoring system and then applying the criteria laid down by the OMGE group to determine whether this was Crohn's or Ulcerative Colitis. As investigations were included as an aid to diagnosis a score of 10 or above was taken as the definition of a case of Crohn's while a

score of < 10 placed the individual in the group classified as Ulcerative Colitis. All this diagnostic information was entered onto a Registration form.

If an individual was deemed to have Crohn's disease further information relating to epidemiology, radiology, pathology, endoscopy, biochemistry / haematology and treatment was collected on the Register's main questionnaire (Appendix 5). This information was also extracted from the patient record.

Once the questionnaire was complete all the information was entered into the computer system.

The few individuals who did not meet the recognised diagnostic criteria but in the view of both the clinician managing the case and myself were thought to have Crohn's disease were also entered into the Register. Those who did not have Crohn's disease were classified as either bowel related disease or as totally inappropriate coding and no other information collected.

Calculated figures for the Crohn's population plus the accuracy of diagnosis are fully discussed in chapter 5.

2.3 THE COMPUTING ASPECTS

2.3.1 Design philosophy

The development of a computer system is a complex task. Ideally the problem should first be defined and then broken into smaller sections for detailed consideration. An overall specification can then be compiled of the functions the system must perform. At this stage decisions can be made about the software design and hardware requirements. Inevitably the final choice will be a compromise between costs, availability, speed of operation and even personal preference.

The overall design philosophy of the system was therefore based on

a) what the system was required to do ?

and bearing this in mind

b) how this would be best achieved ?

Following this strategy it was imperative first to decide on the requirements of the system from a clinical viewpoint. It was then possible to look at the available computing options, both hardware and software, that would meet this clinical need. Having explored the various alternatives a decision could then be taken on the minimum, or perhaps optimum, hardware and software requirements which would permit the development and implementation of the proposed system.

2.3.2 Clinical aspects of computer development

The objective of the eventual prospective system was to produce a dynamic picture of Crohn's disease in Tayside. This would increase the understanding of the disease, provide a disease audit and, if designed correctly, help in patient management. Facilities would obviously be required to record data on the system in a structured relationship so that for instance the diagnostic information belonging to a patient was

linked to epidemiological, investigation and treatment data and vice versa. Similarly it would be important that update information (ie further radiological investigation, treatment etc.) was linked to existing data in chronological order. If this were accomplished an on-going follow-up case record would be created in date order similar in concept to and hopefully more accessible than existing medical records.

If the computerised Register was to be used for audit, management and research purposes data enquiry, manipulation and analysis facilities would also be essential. These facilities should include a simple look-up and browse facility which would permit hardcopy and screen presentations of data in chronological order. Both numerical and non-numerical analysis facilities would be necessary as a large portion of the collected data was non-numerical. The potential value of the register as a prospective management tool would be greatly enhanced if a 'mailmerge/report' facility was also incorporated into the system to enable letters and reports to be generated incorporating the names, addresses and other data taken from the files.

Finally and importantly a mechanism for categorising or subdividing the subjects would be required. This 'subset' structure would enable specific groups of individuals to be selected for closer examination and analysis - for instance those over 60 years at diagnosis or those with symptoms for over 12 months. Secondly by creating subsets in this manner it would be possible to generate letters and reports for specific groups on the register - an important feature if the register was to be developed in a prospective fashion when one might wish to write to a particular group of patients or their general practitioners.

2.3.3 Aspects of hardware and software development

Bearing in mind the clinical requirements of the Register several points required investigation before undertaking the development of the system.

1. Hardware available / required
2. Operating system
3. Database system
4. Software to manage the Register

a) Hardware

The choice of hardware for the project was constrained by the availability, cost and possible future developments.

Within the Faculty of Medicine Computing Unit (FMCU) it was possible to obtain access to the University Dec 10 mainframe computer, however there were limitations relating to access and availability of this machine for clinical purposes.

The Medical Faculty CTL Modular One minicomputer operated by the FMCU had been used for clinical data storage,but this machine was nearing the end of its lifespan and was being phased out in favour of distributed microcomputers connected to a local area network permitting the sharing of peripheral devices such as printers or disc storage media.

The increasing availability of powerful reasonably priced microcomputers both within the FMCU and other hospital departments with their accompanying development potential therefore suggested that this was the most feasible option. The only major drawback of the microcomputer was the uncertainty as to whether a complex register system could be created within the confines of a microcomputer environment.

Finally consideration had also to be given to the medium on which the data was to be stored. The choice here lay between floppy diskette and hard disc media. Although a floppy based system was less expensive the benefits accruing from a hard disc system which included vastly increased data storage capacity and a manifold increase in speed of operation, made it the only real viable option.

Taking these individual points into consideration it was decided to base the development of the computer system on an IBM Personal Computer containing 256Kilobytes of random access memory (RAM) which was linked to the local area microcomputer network and could therefore utilise its hard disc storage medium.

b) Operating System

Before the emergence of MS-DOS as the universally accepted operating system for the IBM PC type microcomputer there were many operating systems such as CPM and AppleDOS in use on a variety of microcomputers. At that time the programming language BASIC was not as developed as it is today and did not readily lend itself to creating large software systems. With the introduction of microcomputers and the local area network the FMCU had opted for a less well known but more versatile operating system known as the UCSD p-system using the language Pascal, many features of which have subsequently been incorporated into dialects of BASIC.

The UCSD operating system had its origins in the University of California at San-Diego where it was developed in the mid 1970's. It was initially developed as a solution to a particular problem within the University Computing Department by Professor Kenneth L. Bowles. Interest, however, soon grew and by the late 70's several implementations had been produced. The developers of these implementations were given three prime design objectives:-

1. should be oriented to the novice but acceptable to the expert.

2. should operate within the confines of a microcomputer environment.

3 must provide a portable software environment to enable programmes to run on different microcomputers.

Although never achieving widespread popular acceptance the p-system is recognised as an ideal design and development tool and as such has been used by many

educational and university establishments and commercial system designers. More importantly however, the three prime objectives laid down by the developers exactly met the criteria of the operating system required to develop the Register.

The UCSD system was developed around an imaginary 'ideal p-machine' which resides between the host computer's own native operating system and the p-system program code files. In short, programmes are written in the p-system Pascal language as text files, compiled into p-code program code files and then run on any microcomputer supporting the p-system. Each microcomputer has its own specific 'p-machine interpreter' which interprets the p-code and enables it to run a program as if it were using its own native operating system. Thus any computer which has a p-system interpreter will be able to run a p-code program without modification.

This system has several important advantages over the more commonly used operating systems. Its use would enable the development of the Register's programmes to proceed on a number of microcomputers within the department and would not therefore tie one machine to this single function. Secondly, and more importantly, the developed programmes would run on any computer that supported the p-system, thus greatly diminishing any future problems of hardware/software incompatibility. Indeed the p-system now being used operates under a number of operating systems as well as the MS-DOS system.

This system does incur an approximate 10% reduction in the running speed of p-code programmes which occurs because the code is interpreted by the p-machine emulator. This compared favourably with many implementations of BASIC available at that time which interpreted the original source code with a manifold reduction in performance.

c) Database

The choice of a database to support the register was restricted to one of three possible options:-

1. buy a commercial package
2. write a dedicated database record structure in p-system pascal
3. use the database system being developed within the department

Commercial packages initially appeared the most suitable for adapting to the Crohn's Register database with packages such as Knowledgeman, D-Base II & D-Base III (Ashton-Tate) and Silicon Office (Bristol) seemingly being readily adaptable to store the Crohn's data. Unfortunately this type of package has several disadvantages. Each is in some way a closed system - the user therefore has no access to the source code and can only utilise the facilities provided within the package. Furthermore most are directed at the business user and are less well equipped to handle medical data much of which is textual in form.

Designing and using a p-system Pascal record structure as the database was briefly considered, however because of the volume of data to be collected this would result in a very large data structure. Secondly because Pascal is a very strictly 'typed' language the record structure would be very inflexible.

Attention was therefore turned to the database system within the department. This database using what is now called the fourth generation principle of conversationally generated record formats with medically orientated data types had been developed and used on the department's mini-computer for several years. The concepts and data types had been well proven, however the rewrite of the system for the microcomputer environment was only at an early stage. In addition new features found necessary from experience with the original mini-computer based system were still to be incorporated.

The main advantage of this database facility was that it had been developed specifically to cater for medical data collection and storage. The data structures within the database were superior and more flexible than those of most commercial packages and coped equally well with non-numerical and numerical data.

Several important concepts and data structures not normally incorporated within commercial database packages were contained in this system. Examples of those thought to be of special value within the Crohn's register are described below.

The data field type 'multiple coded response' enabled the user to choose several codes from a defined repertoire and enter them all in one data field. For example for the question 'What were the histological findings ?' one could enter a string of codes 'ABG' where each character represented one particular finding for instance acute inflammation, chronic inflammation and giant cells. In addition the system provided full text expansion of input codes for example replying 'A' to the above question caused the expanded text for that code to be displayed on the screen - 'acute inflammation' in the above case. This greatly aids the accuracy of data input by giving immediate feedback of the coding system.

Another field type, the 'conditional' or 'logical' type, enabled the streaming of data input. Thus answering 'Y' to the question 'Did the patient have an operation ?' would then prompt the user to answer questions on the type of operation, date of operation, reason for operation and diagnosis at operation while answering 'N' would by-pass all these irrelevant questions.

Furthermore validity checking on input was an integral part of the system and is essential if invalid or meaningless information is to be trapped before it is filed away. This is important because the main weakness of any computer system is the user/keyboard interface; once data has been entered into a system it is very difficult to check its accuracy and validity.

Therefore despite the drawbacks associated with developing a software application based on an untried database it was felt that the advantages of using this system far outweighed the potential problems. As will become evident this decision has been fully vindicated.

d) Software Development

Two approaches to the software development were considered

1. To write a suite of programmes that were dedicated to the operation of a functioning Crohn's disease Register.

2. To develop a collection of programmes as a set of tools which could be used subsequently to support other similar applications using the department's database system. The facilities required for full operation of the Crohn's Register were substantial and could be used as an initial pilot in the development of a general purpose system.

The dedicated program solution appeared at first sight to be the more attractive and less complicated option. However further thought and initial development suggested that the large number of data fields being collected would create considerable programming difficulties when it came to data enquiry and analysis routines.

At this time increasing demands were being placed on the medical computing unit for microcomputer based data collection and management facilities as the numbers of microcomputers increased within the district. Moreover with the recent demand for audit within the Health Service accompanied by the significant reduction in costs of microcomputer technology it was clear that demand for this type of system would continue to increase significantly. Finally the new microcomputer systems were intended to act as a replacement system for the faculty's mini-computer when it was eventually withdrawn from service. Because the data structures would be of similar format it was

anticipated that data would be transferable from the old system to the new thus retaining the value of data sets which had been collected over many years.

The benefits that might accrue from such a general system were therefore not inconsiderable and indeed were one of the aims the author had proposed in application for the SHHD computing fellowship which had been obtained to support this work. It was therefore decided to develop a suite of programmes around the facilities required by the Crohn's Register. The programmes would be written so that they addressed the data field types as opposed to specific field numbers. This would have the effect of laying the foundations from which a general database management system might evolve. The development and implementation of the Register is now discussed in some detail.

CHAPTER 3

THE COMPUTERISED REGISTER

3.1 DATABASE FILE STRUCTURE FOR THE DISEASE REGISTER

The data to be collected fell into two distinct categories: non-recurrent (ie date of diagnosis) and recurrent (ie investigations and operations). Because large recurring data sets consume large amounts of computer memory it was decided to break the data set into data files of more manageable size thus saving on both memory within the computer and on its associated data storage medium. The data set was conveniently divided into 4 data files - 2 files containing non-recurring data, Diagnostic and General information, and 2 with recurring data, Investigation and Treatment/Morbidity data. A data file can contain a maximum of 32,000 records with each record comprising the data items related to that particular file. The diagnostic file for example could therefore grow to a maximum size of 32,000 records (or 32,000 patients) each containing 33 separate items of diagnostic information.

A subject entered into the register could have data records in all the data files and would therefore require an 'index structure' to link all his or her data records together. To achieve this link the concept of a 'Control file' was created. Each individual entering the Register was assigned a unique record in the control file which acts as an index to all that patient's data file records. This file was generated to permit up to 32 records or follow-up visits for each of the four files to be linked to a subject. This record was also to contain other important information relating to the subject's unique register number, subset membership (see page 49) and certain important dates (Fig 3.1).

In summary the Register's database file structure consists of a Control file in which each subject has one record which indexes the data records in each of the 4 data files and contains subset and other 'housekeeping' information (Fig 3.2).

A CONTROL FILE RECORD

subject number (0 to max study number)

INDEX	file 1	1	45	90	98	126	
to the	file 2	76	77	each number points to a			
data	file 3			record in the data files			
files	file 4	27	98				

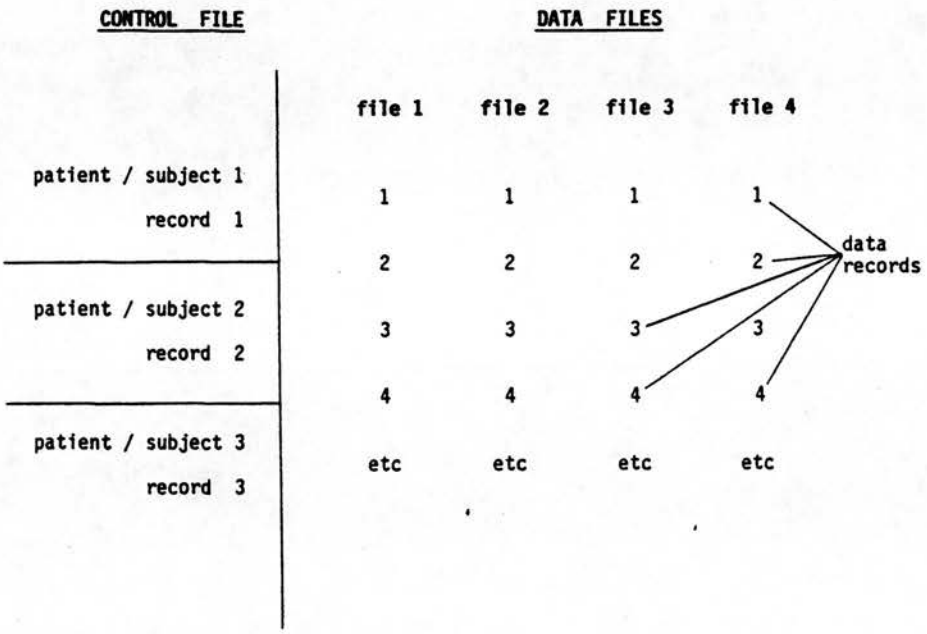
Subset	type 1	+	-	(if + patient in subset)			Max 32
markers	type 2	+	+	-	-	-	Max 16
	type 3	-	-	+	+	+	Max 16

Date subject registered 1. 3.85

Date last had data entered 3. 6.86

Format of control record

Figure 3.1



1 control file per study data files (Max of 4 per study)

Each subject has 1 record in the CONTROL file containing record numbers which point to record in the DATA FILES

(control file acts as an index to the data file records)

General system structure

Figure 3.2

3.2 PROGRAMME DEVELOPMENT

The suite of programmes required to generate the Crohn's register were developed in a modular fashion. This modular approach enabled each programme within the system to be generated independently and made the overall development more logical and manageable.

Three main programme modules were created

1. Generation of the Register
2. Input of data to the register
3. Data enquiry and analysis.

In order to enable non-computer personnel subsequently to use the computer facilities the control programme module has been created in such a way that it is 'menu driven'. This enables those with no experience of the system to be led through the facilities by answering simple questions. A 'help' facility has also been incorporated in order to assist those who are not familiar with the operation of the system. This offers a short and concise description of the options presented in a particular menu to be called up if a user finds the simple menu unclear.

3.2.1 Generation of the Register

This module was designed to generate the database to the Register's specification. The programme was developed as a 'user friendly' interface to the data file generator programme already existing in the department and permitted the generation of the four data files associated with the register plus the control file structure.

Each data item was configured into a data field in the appropriate data file by answering a series of simple questions related to:

a) type of data (e.g. number, date, string characters, coded response or logical formats)

b) question to be displayed on screen (e.g. Date of birth)

c) range of codes/values permitted (e.g. max & min ranges).

Each of the four data files was generated in a similar manner and then named appropriately:

cr_diag.dat	33 fields
cr_gen.dat	68 fields
cr_inv.dat	36 fields
cr_marx.dat	34 fields.

Once the data files had been generated the control file was created by answering an additional set of simple questions.

3.2.2 Input of data to the Register

To achieve the intended goal of a dynamic register in which patient events and data input were related to time several different forms of input pathway were required. The four main input pathways were :-

1. Registration
2. Update
3. Modification
4. Deletion.

The registration or take on of a subject to the register occurs only once. After a subject has been registered information contained within his or her data records may require modification for instance changes in name/address or change of general practitioner. Update of a subject's data will occur when new information is added and associated with that subject's existing data. A deletion pathway was also included to

enable correction of catastrophic user mistakes.

Once again it must be stressed that data input is a weak link of any computer system. Once data has actually entered a database it is very difficult to check either its validity or accuracy. To reduce this type of operator error validity checking has been incorporated within each data field, thus if a Haemoglobin (Hb) value of >20 is entered into the Hb data field the system will reject the value and prompt a further reply. This form of checking will prevent totally inappropriate data from being entered, however it will not prevent the input of valid but inaccurate data (ie entering a Hb value of 11 rather than 13). To help avoid this type of error all data entered is redisplayed on the screen for checking - an option is also available to modify incorrect data before sending it back for storage. Subsequent analytical audit of the data can also be used to seek out some of this type of error if it can be detected as being contextually inconsistent.

To maintain efficiency with data transactions the concept of an 'Input form' was introduced. These input forms select the questions necessary to carry out particular data transactions. The following forms are at present used for the register.

a) Registration

b) Investigation

c) Treatment

The 'Registration form' will only display questions and prompt answers for the data fields which relate to registration. Similarly the 'Investigation form' contains information on data fields which relate to investigations. This form has been further classified into 5 sub-forms or sections each concerned with one type of investigation

1 radiology

2 pathology

3 haem/biochem

4 endoscopy

5 all investigations.

These mechanisms greatly reduce the time required for input by eliminating as many unnecessary questions as possible. For subsequent prospective operation and maintenance of the Register this is an important factor.

To summarise, all data entering the Register system must pass through the above input pathways. The order and sequence of data input is optimised by the generation of 'Input forms' which can be created, altered and deleted as required to match operational circumstances.

3.2.3 Data management facilities

Once data has been entered into the Register any of the management facilities contained in the system may be used to enquire, manipulate and/or analyse information in the database.

The management menu is displayed below :-

1. Subsets
2. Data analysis
3. Browse and Print
4. Letters & Reports
5. File information
6. Sorter routine

Each of the headings represents a different utility which can be performed on data within the Crohn's Register.

Subsets

The concept of subsets has already been introduced. This permits individuals within the Register to be grouped together because they all meet certain 'criteria', for example all the males, all those under 30 at diagnosis, all those with a five year follow-up. Once a subset has been created it can be named and then saved to disc

(fig 3.3). All other management facilities can then utilise one or more of these subsets as a cohort for further analysis, enquiry and report generation.

Although a maximum of 64 subsets can be held within the system at any one time each can be deleted and regenerated at any time. Once generated subsets can also be compared with each other to create more specifically defined groups; the 'males' subset may be compared with the '>60 at diagnosis' and 'large bowel disease' subsets thus creating a new subset of all the males who are over 60 at diagnosis and have large bowel disease.

A number of conditional constructs have been created to define the criteria for membership of a subset

1. manually entering patients with specified criteria which have not been collected in the database (ie those with ginger hair).
2. specific criteria (ie all the females or those with Hb < 10 gms/dl) with up to 4 conditions specifiable each time.
3. related to the number of register entries each subject has (ie the third visit / entry)
4. from the subtraction of dates or numbers (ie all those with no recurrence for 5 years / those who were not diagnosed as Crohn's until 1 year after presentation).

The subset concept provides great flexibility to the system enabling the creation of cohorts or sub-populations which can then be used to submit recognised groups of subjects to other register utilities for research, audit and management purposes.

Data analysis

Like a great deal of medical information the Crohn's database contains a large proportion of non-numerical data items. To analyse the numerical data a suite of standard statistical tests was incorporated into the system. A special tabular format was devised to display non-numerical data in a numerical fashion. Database analysis utilities

SUBJECT CONDITIONAL SUBSETS

1	Females (188) 19/1	2	Males (128)
3	>= 60 at diag (35) 19/1	4	not made
5	<20 at diag (52) 19/1	6	diarrhoea 203
7	<60 at diag (278) 19/1	8	<= 30 at diag 154
9	40 to 59 at diag (65) 20/1	10	20 to 39 at diag (161) 20/1
11	Sm. Bowel Dis (97) 21/1	12	Ileo-colic dis (94) 21/1
13	Large bowel (71) 21/1	14	Discontin Dis (44) 21/1
15	pain 220	16	wt loss 173
17	not made	18	PR bleeding 50
19	gross fd/crohns 172	20	females+biopsy 132
21	biopsy/crohns 72	22	granuloma all (157)
23	males & biopsy 93	24	Transmural all (85)
25	not made	26	crypt absc all (50)
27	not made	28	giant cell all (95)
29	not made	30	Radiol Crohns (189)
31	Path diag 226	32	not made

Choose which condition

Subsets

Figure 3.3

were therefore developed to provide

a) Non-numerical data presentation and analysis

b) Numerical statistical analysis.

Non-Numerical Analysis

The one and two dimensional table format was chosen as the method of representing this type of data. All field types can utilise this analysis facility. Fields may be analysed singly or in pairs. Typical examples of this flexible analytical technique are shown in figs 3.4, 3.5, 3.6 and 3.7. Figures 3.4 & 3.5 show a single field analysis (sex ratio) and comparison of two fields (sex ratio against site of disease). Figure 3.6 presents the changing haemoglobin values of those in the register over sequential visits and finally figure 3.7 represents the analysis of one field, the site of disease, against several previously defined related subsets - in this case age at diagnosis.

Furthermore the ranges or intervals into which each parameter can be divided can be varied. The system defaults to generating equal ranges for any field type being analysed - for instance the Haemoglobin field will have 8 ranges generated starting at 5 and incrementing by 2 to create each new range - however these can be overridden and chosen to suit a particular analysis. For example the analysis of the Hb field would perhaps be more appropriately analysed in three ranges (5-<10gms/dl, 10-<12 gms/dl and above 12gms/dl) especially when the data to be analysed is likely to be skewed.

Numerical Analysis

In order to provide standard statistical facilities for numerical data a suite of standard statistical paired and unpaired tests have been included which can operate on

TABULAR PRESENTATION AND ANALYSIS

Sex

317 data points from a Sample of 317 subjects

Sample is from a population of 319 selected from ALL subjects

KEY for Y axis

Field 15 in File crohns:cgen - SEX

1 = MALE

2 = FEMALE

		1
	N!	1
?	%C!	0%T
	N!	128
1	%C!	40%T
	N!	188
2	%C!	59%T

TOTAL! 317

N = number
? = empty fields

%T = % of Total
%C = Number as % of Column total
%R = Number as % of Row total

Simple analysis

Figure 3.4

TABULAR DATA PRESENTATION AND ANALYSIS

Sex & Site of Disease
317 data points from a Sample of 317 subjects
Sample is from a population of 319 selected from ALL subjects

KEY for X axis
Field 36 in File crohns:cinv - **EXTENT DISEASE**
A = SMALL BOWEL
B = ILEO COLIC
C = LARGE BOWEL
D = DISCONTIN DISEASE

KEY for Y axis
Field 15 in File crohns:cgen - **SEX**
1 = **MALE**
2 = **FEMALE**

		?	A	B	C	D	TOTAL
	N!	0	0	0	0	1 !	1
?	%R!	0.0	0.0	0.0	0.0	100.0 !	
	%C!	0.0	0.0	0.0	0.0	2.3 !	0%T
	N!	5	46	35	26	16 !	128
1	%R!	3.9	35.9	27.3	20.3	12.5 !	
	%C!	45.5	47.4	37.2	36.6	36.4 !	40%T
	N!	6	51	59	45	27 !	188
2	%R!	3.2	27.1	31.4	23.9	14.4 !	
	%C!	54.5	52.6	62.8	63.4	61.4 !	59%T
	TOTAL!	11	97	94	71	44 !	317
	%T!	3.5	30.6	29.7	22.4	13.9	

N = number
% = empty fields

%T = % of Total
%C = Number as % of Column total
%R = Number as % of Row total

Two dimensional analysis

Figure 3.5

TABULAR DATA PRESENTATION AND ANALYSIS

Hb values 1st five visits

1050 data points from a Sample of 317 subjects

Sample is from a population of 319 selected from ALL subjects

KEY for X axis

A = 1
B = 2
C = 3
D = 4
E = 5

} visit

KEY for Y axis

Field 15 in File crohns:cinv - HB

1 = 5 TO 9

2 = 10 TO 11

3 = 12 TO 19

		?	A	B	C	D	E	TOTAL
	N!	0	44	143	165	136	90 !	578
?	%R!	0.0	7.6	24.7	28.5	23.5	15.6 !	
	%C!	0.0	13.9	51.3	76.0	92.5	100.0 !	55%T
	N!	0	12	7	2	0	0 !	21
1	%R!	0.0	57.1	33.3	9.5	0.0	0.0 !	
	%C!	0.0	3.8	2.5	0.9	0.0	0.0 !	2%T
	N!	0	76	36	8	1	0 !	121
2	%R!	0.0	62.8	29.8	6.6	0.8	0.0 !	
	%C!	0.0	24.0	12.9	3.7	0.7	0.0 !	12%T
	N!	0	185	93	42	10	0 !	330
3	%R!	0.0	56.1	28.2	12.7	3.0	0.0 !	
	%C!	0.0	58.4	33.3	19.4	6.8	0.0 !	31%T
	TOTAL!	0.0	317	279	217	147	90 !	1050
	%T!	0.0	30.2	26.6	20.7	14.0	8.6	

N = number

? = empty fields

%T = % of Total

%C = Number as % of Column total

%R = Number as % of Row total

Analysis by Clinic visit

Figure 3.6

SINGLE FIELD ANALYSIS USING SUBSETS

TABULAR DATA PRESENTATION AND ANALYSIS

Site of disease

307 data points from a Sample of 307 subjects

Sample is from a population of 319 selected from 4 Subsets

KEY for X axis

Code and subset name

A = Hb <10 (12)

B = WCC >10 (127)

C = Protein <60 (65)

D = Albumin <34 (103)

KEY for Y axis

Field 36 in File crohns:cinv - **EXTENT DISEASE**

1 = SMALL BOWEL

2 = ILEO COLIC

3 = LARGE BOWEL

4 = DISCONTIN DISEASE

		?	A	B	C	D	TOTAL
?	N!	0	0	0	1	1 !	2
	%R!	0.0	0.0	0.0	50.0	50.0 !	
	%C!	0.0	0.0	0.0	1.5	1.0 !	1%T
1	N!	0	2	43	27	36 !	108
	%R!	0.0	1.9	39.8	25.0	33.3 !	
	%C!	0.0	16.7	33.9	41.5	35.0 !	35%T
2	N!	0	5	41	14	24 !	84
	%R!	0.0	6.0	48.8	16.7	28.6 !	
	%C!	0.0	41.7	32.3	21.5	23.3 !	27%T
3	N!	0	2	30	14	23 !	69
	%R!	0.0	2.9	43.5	20.3	33.3 !	
	%C!	0.0	16.7	23.6	21.5	22.3 !	22% T
4	N!	0	3	13	9	19 !	44
	%R!	0.0	6.8	29.5	20.5	43.2 !	
	%C!	0.0	25.0	10.2	13.8	18.4 !	14% T
TOTAL	N!	0	12	127	65	103 !	307
	%T!	0.0	3.9	41.4	21.2	33.6	

N = number
? = empty fields

%T = % of Total
%C = Number as % of Column total
%R = Number as % of Row total

Analysis by subsets

Figure 3.7

the data files. The tests presently available are :-

Means & standard deviations

T-tests

Percentiles

Mann-Whitney

Regression analysis

Wilcoxon signed ranks

Kendalls correlation

A file and field number are defined by the user and the data loaded into the statistics programme either for the whole file or for a particular previously defined subset. Data may also be entered manually so that the analysis facilities may be used as a stand alone statistical package. Once loaded the values may be saved in a file on disc for later use. Outlying or skewed values may be excluded and various data transformations may be performed prior to processing.

The data analysis section thus provides two separate and powerful analytical tools which between them will analyse any data item stored within the register. The numerical analysis facilities may be insufficient to explore some complex relationships to which end a utility has been developed to convert the system's numerical values into a format that can be transferred to more sophisticated statistical packages running on mini or mainframe computers.

Data enquiry and Print facilities

This facility has been included to permit simple data enquiry operations either for presentation on the screen or as hardcopy. The function allows the operator to choose any field or group of fields within the register and then display all the data relating to those fields, on the screen or printer, for an individual or subset of individuals. The facility therefore enables the user to examine sequentially an individual's radiological or

haematological/biochemical tests over a period of time. In the same way a summary of an individual's clinic attendances can be presented. These facilities are of considerable value in presenting a concise summary of one aspect of a patient's record for clinical management decision making.

Letters and Reports

To help in the prospective management and retrospective data enquiry a 'mailmerge' utility has been incorporated as an integral part of the computer system. This section includes a basic word processing unit which permits letter or report templates to be created. By using specific symbols within the template (fig 3.8) information can be drawn from the Registers database to generate a personalised letter or report (fig 3.9).

A 'bank' of standard letters and reports can be prepared for use in producing recall letters to patients and general practitioners, clinical summaries, extra questionnaires etc.

Other utilities within the register

Other general housekeeping functions have been included to help in the running of the register. These include an enquiry facility to examine the structure and content of both the data and control files. A 'sorting' option has also been included which will sort any field type alphabetically or numerically thus permitting the generation of lists of patients either alphabetically or in date of birth order.

Gastroenterology clinic
Ninewells Hospital
Dundee
{*}

Dear Dr $2:9:0:1$,
This patient of yours $2:3:0:1$ $2:2:0:1$
$2:6:0:1$
$2:7:0:1$
$2:8:0:1$
has not been seen at the Gastroenterology clinic since $4:19:0:-1$ and has failed to attend 2 appointments since this date. We would be grateful if you could advise us as to $2:15:0:1{1}$ whereabouts and/or $2:15:0:1{1}$ general condition.

Yours Sincerely,

Michael Walker
Registrar Gastroenterology clinic

Example of Letter TEMPLATE

Figure 3.8

Gastroenterology clinic
Ninewells Hospital
Dundee
23.4.85

Dear Dr Patterson,
This patient of yours David Williams
23 Thurso Cres
Dundee

attended for a Barium meal and follow-through

on the 20.4.85.

Findings: irregularity
narrowing
ulcers

Site: ileum
ascending colon

Diagnosis: Crohns disease

He will be seen shortly in the clinic to discuss this result.

Yours Sincerely,

Michael Walker
Research Registrar

Example of sample REPORT

Figure 3.9

3.3 USING THE REGISTER'S FACILITIES

Creation of the Crohn's database in the proposed format using the generator programme confirmed the feasibility of developing the computerised register within a microcomputer enviroment. The data input software was then fully tested by entering the information that had been collected on the retrospective data forms. Appropriate 'input forms' were created to expedite the retrospective data entry. This retrospective data input proved a lengthy task and revealed a number of 'bugs' and potential operator frustrations which were subsequently removed.

Once the retrospective database take-on had been completed attention was turned to the management facilities. Many of the facilities required in the operation of the prospective register were also required for analysis and enquiry of the retrospective information and therefore provided a good test for them. The findings of the enquiry and analysis of the retrospective database are described in the following chapters. These have been compiled mainly using the subset, analysis and printout routines, however in addition Students t-test and Chi^2 tests have been used for some simple numerical analysis. This retrospective analysis has proven the data manipulation facilities to be both flexible and valuable in operation.

Several important additional enhancements have been incorporated into the system as a result of this initial use. An example was the requirement to create a subset 'manually' using criteria which were not recorded in the database - for instance a group with a cow milk allergy. It was also found necessary to permit the comparison and analysis of a field using several existing subsets (fig 3.7). Further additions and refinements to the software continue, the system evolving as its use continues both in the form of the Crhn's Register and through its wider application.

The pilot study has therefore shown the computerised Register to be both versatile and easy to use and demonstrated the value of the facilities included within the system.

CHAPTER 4

CHECKING THE VALIDITY OF THE REGISTER

4.1 COMPLETENESS OF CASE ASCERTAINMENT

Before embarking on epidemiological analysis of the retrospective data it was, as previously noted, essential to check the validity and accuracy of the data.

In chapter 3 the method of case ascertainment and cross checking was described in some detail. Table 4.1 shows the number of possible cases derived from each of the sources used.

Tayside Community Health Index (CHI) 1974-83	394
Scottish Morbidity Returns (SMR1) 1968-74	99
General Practitioners	43

Table 4.1 Sources used in initial case capture

Possible cases of Crohn's were initially obtained from computer listings from the Tayside CHI (1974-83) and SMR1 returns (1968-73) respectively. Each individual listed was then subjected to the Register's scoring system before being considered a confirmed case of Crohn's disease. In June 1985 each general practice in Tayside was contacted and asked to ratify that those patients who had been identified as being on their practice list and confirmed as Crohn's disease were still under their care. By leaving this 18 month gap it was hoped to pick up patients who may have had symptoms from 1983 or before but were not diagnosed until post 1983 or had not had a hospital admission for their disease before that time. Secondly the General Practitioner's were asked to include on their reply form any additional individuals who were under their care and whom they considered to be suffering from Crohn's disease.

This procedure revealed only a further 16 individuals with genuine Crohn's disease who did not already appear within the Register.

Prior to 1979 routine mortality statistics did not differentiate deaths from Crohn's disease from that of Ulcerative Colitis and other chronic enteritis. Since this time Crohn's mortality statistics have been collected separately and have shown between 6 to

30 deaths each year in Scotland. The Tayside figures support the low mortality suggested by the Scottish figures; only 11 patients were considered to have Crohn's disease as a primary cause of death over the 16 years of study. Crohn's disease was considered a secondary cause of death in a further 23 patients dying during the period of study.

Computerised statistics from the Pathology department were also examined for the years 1976-83. Although it was not possible to identify all those with a diagnosis of Crohn's disease - using systematised nomenclature of pathology (SNOP) -because of inadequate and inaccurate labelling of specimens no new cases of Crohn's were uncovered. Furthermore a positive pathological diagnosis is often difficult with terms such as 'consistent with Crohn's disease' or 'impossible to exclude Crohn's' being understandably common. Use of such statistics without validity checking might therefore prove unreliable.

4.2 ACCURACY OF ICD CODING IN TAYSIDE

As it was intended to base the initial case capture upon inpatient ICD codes for Crohn's disease it was essential to check the accuracy of the coding for Crohn's and related conditions (eg. Ulcerative Colitis and Non-Specific Colitis). This would provide some measure of the number of patients with Crohn's disease that might be missed if the Crohn's ICD code were the only method of case capture used. To test the accuracy of ICD coding within Tayside for Crohn's and similar diseases a small pilot study was set up to examine the accuracy of initial in-patient coding. Three groups of 50 patients each from Tayside district who had been classified as Crohn's disease (ICD = 550), Ulcerative Colitis (ICD = 556) and Non-Specific Colitis (ICD = 558) were picked from the Tayside inpatient CHI computer diagnostic listings for 1980-81. Each group consisted of the first 50 individuals from the district who had been given one of the three relevant ICD codings. The progress of each of those patients was monitored retrospectively through their out-patient clinic visits following their discharge. Each patient therefore had at least three years of follow-up during which the original diagnosis could be confirmed or altered. All patients initially identified were traced over the three year period. Table 4.2 reveals that the initial ICD diagnostic codes for these groups were accurate in 76%, 90% & 87.5% for Crohn's, Ulcerative Colitis and Non-Specific Colitis respectively even after a three year review period.

		Number with disease after 3 years of follow-up		
Inpatient ICD Code	N	Crohn's disease	Ulcerative colitis	Non specific colitis
Ulcerative Colitis	47	1	42	4
Non-Specific Colitis	48	3	3	42
Crohn's disease	50	38	5	7

Table 4.2 Accuracy of inpatient ICD Coding after 3yrs Follow-up

These diagnostic results were derived from information obtained on the patients over the three year period. They compare the initial coding diagnosis with the actual diagnosis three years later and do not take into account the relative accuracy of the initial diagnosis. The figures are therefore a measure of the accuracy of the initial diagnostic coding after three years of follow up.

The results of this small study therefore indicate that even after a 3 year follow up period following hospital admission only 2% of those initially thought to have Ulcerative Colitis and 6% of those classified as Non-Specific Colitis will be found to have Crohn's disease. While these figures do not take into account patients who might yet develop Crohn's disease there was no evidence from examination of the case records to suggest that any of the remaining Non-Specific Colitics might have Crohn's disease. The Ulcerative colitics were however more difficult to assess. Each patient from this group was submitted to the scoring system suggested by the OMGE group and all had a total score suggesting Ulcerative Colitis and not Crohn's disease.

These findings imply that some patients would be missed if case ascertainment was based solely on Crohn's ICD codings. The numbers missed because of incorrect coding would however appear to be small because even after three years of follow up only 4% of patients have had their initial ICD code revised to one of Crohn's disease. More importantly of those that were revised through follow up visits all were subsequently classified with a Crohn's ICD code from a successive admission.

More significantly the pilot study revealed a marked variation in the number of false positives (ie those thought to have the disease initially but subsequently found not to have Crohn's disease) between the three groups (24% in Crohn's, 12.5% in Non-Specific Colitics and 11% in Ulcerative Colitic groups respectively). These figures confirm the findings of other groups from Glasgow (Smith 1975) and Northern Ireland (Humphreys 1975) who found a large percentage of inpatients coded as Crohn's disease did not have the disease - approximately 50% in each study. It was therefore felt that even

though there would likely be a large number of false positives if case ascertainment was based purely on Crohn's inpatient ICD coding it would provide a valid population on which to base the initial screening.

4.3 ACCURACY OF DIAGNOSTIC METHOD

To test the validity of the Register's diagnostic methodology the sensitivity, specificity and predictive value were calculated for the Crohn's, Ulcerative Colitic and non-specific Colitic groups respectively.

Every individual from each of the groups was submitted to the Register's diagnostic criteria firstly for Inflammatory Bowel Disease (IBD) and then Crohn's or Ulcerative Colitis. The results of step 1 - the diagnosis of IBD - are displayed in table 4.3.

	N	no. with disease	not bowel disease	false +ve	false -ve
Crohn's disease	50	42	2	1	5
Ulcerative Colitis	47	42	4	0	1
Non-Specific Colitis	48	3	42	0	3
	--	--	--	--	--
All	145	87	48	1	9

Table 4.3 Accuracy of Inflammatory Bowel Disease scoring system

The diagnosis of IBD by the register's criteria was based on a score taken from the addition of a maximum of 4 criteria - clinical symptoms, radiological, pathological and endoscopic findings. To obtain the diagnosis of inflammatory bowel disease the individual was required to have at least half of the performed investigations relating to possible IBD showing some positive evidence of disease, and must have a total score of 6 or more when adding the symptom score to the investigation score.

Of those 145 patients submitted to step 1 of the diagnostic procedure 87 were found to have IBD, there was 1 false positive, 9 false negatives while 48 did not have IBD. This test on its own gave a sensitivity of 91%, a specificity of 98% and a predictive value of 98%.

The OMGE group found a predictive value of 93% for their scoring system used to separate Crohn's disease from Ulcerative Colitis. To test whether our

interpretation and application of the scoring system was comparable, the 50 Crohn's patients and 47 Ulcerative Colitic patients were checked to see whether our predictive value was similar to the OMGE group. Taking those individuals who had passed the initial diagnostic test for IBD from the Crohn's and Ulcerative Colitic groups and then applying the OMGE criteria we found that of the 90 patients (47 Crohn's / 43 Ulcerative Colitis) submitted to the test 43 had Crohn's, 42 had Ulcerative Colitis, there were 4 false negatives and 1 false positive. This serial investigation gave a sensitivity for Crohn's disease of 91%, a specificity of 98% and a predictive value of 98%. The overall accuracy of the test for Ulcerative Colitis or Crohn's disease was 94%.

This type of serial testing is recognised to maximise the specificity and positive predictive value although reducing the sensitivity of diagnostic testing.

Despite the small numbers examined the figures suggest that by using this method the probability of obtaining the correct diagnosis of Crohn's disease has been slightly increased compared to the method described by the OMGE group.

4.4 ACCURACY OF DIAGNOSIS IN POTENTIAL CROHN'S POPULATION

Taking SMR1 and Tayside CHI returns produced a total of 493 individuals who had at least one occurrence of an ICD coding for Crohn's disease. Table 4.4 reflects the actual diagnosis of those described as Crohn's disease by Tayside SMR1 and CHI returns.

	confirmed Crohn's	not Crohn's disease	notes not traced
diagnosis from CHI (1974-83)	260	106	12
diagnosis from SMR1 (1968-73)	42	49	24

Table 4.4 Accuracy of inpatient ICD Coding

Only 65% of those with an ICD coding of Crohn's disease had proven evidence of the disease while 7% of case records could not be traced and therefore diagnosis neither confirmed or refuted. These figures indicate that the accuracy of ICD coding for Crohn's disease in Tayside is poor although table 4.5 suggests that it has improved over the years examined.

	(positive predictive value)	
1968-73	1974-83	1980-81
46%	71%	76%

Table 4.5 Probability of true Crohn's diagnosis from ICD code

Out of a total of 90 Primary Care practices in Tayside all replied to the questionnaire posted to them. Only one single handed practice refused to confirm or add

to the data supplied because of possible contravention of the data protection act. The replies resulted in a further 43 patients being added to the list of potential Crohn's patients who had been identified from SMR1 and CHI returns (Table 4.6).

	confirmed Crohn's	not Crohn's	no trace records	diagnosed after 1983
Diagnosis from GP (43)	19	14	5	5

Table 4.6 GP Diagnostic pick up

Of the 19 cases that were confirmed 3 already appeared in the Register having been entered while registered with a different practice. In retrospect it would also have been of value to determine the number of individuals that met the Registers diagnostic criteria for Crohn's disease but were not known to the general practitioner as sufferers of the disease. Unfortunately the questionnaire was not laid out in a manner that this data could be obtained.

A breakdown of the 169 labelled as Crohn's who did not meet the Registers diagnostic criteria is shown in table 4.7

79	inappropriate / incorrect diagnosis
18	acute ileitis
72	related diagnosis

Table 4.7 Breakdown of incorrect ICD coding

The reasons why so many had an inappropriate diagnosis is unclear, however in this group no information could be found in the case records to give any hint of IBD. This suggests that the errors were made either in identifying the ICD code or in the transcription to the SMR1 form.

Overall 536 individuals were identified as possible cases of Crohn's disease during 1968-83. In 41 (7.6%) of this group the diagnosis could not be confirmed or refuted because no information could be found to check the diagnosis. Of the remaining 495 patients in whom it was possible to check the diagnosis 318 (64.2%) patients met the Register's diagnostic criteria and were admitted to the Register.

Further examination of those admitted to the Register showed that 92% passed the diagnostic criteria for IBD with the mean score being 9.0 (range 1-18) while the median was 9.0. More importantly however table 4.8 shows the numbers of Crohn's patients with radiological, endoscopic or pathological evidence of disease. Patients with specific types of investigation performed were 'scored' on three levels. Those having no evidence of disease and those having enough evidence to confirm the presence of IBD. Individuals considered to fall between the two extremes were described as having some evidence to support a diagnosis of IBD.

Of those entered into the Register 271, 193 and 267 had a radiological, endoscopic or pathological investigation performed respectively prior to diagnosis.

The interpretation of written reports and case records by the author and the interpretation of the investigations performed by the clinicians is of course open to observer variation. The OMGE group were surprised at the uniformity of the interpretation of the diagnostic proforma used in their study and also suggested that the majority of clinicians were in agreement as to what constituted a case of Crohn's disease or Ulcerative Colitis in the great majority of patients. With this in mind it was felt that the author would likely fit into the same category as the majority of clinicians and that observer error in this part of the diagnostic system would not be important. Error on the part of clinicians performing investigation and the author's interpretation of the results was also open to observer error. The diagnostic criteria used in the study were based on a number of different types of observations and investigations. It was felt that an error in one observation would be offset by the many other observations involved in reaching a

diagnosis; using this form of serial observation should therefore reduce the likelihood of an incorrect diagnosis.

	Radiology		Endoscopy		Pathology	
not performed	46	(15%)	124	(39%)	50	(16%)
no evidence	60	(15%)	88	(28%)	43	(14%)
some evidence	55	(17%)	19	(6%)	13	(4%)
good evidence	156	(49%)	86	(27%)	211	(66%)

Table 4.8 Types of Investigations prior to diagnosis & evidence of disease

All patients registered as having Crohn's disease had some gastrointestinal symptoms of the disease at the time of diagnosis. The most common number of symptoms at the time of diagnosis was 4 - few had 6 or more abdominal symptoms (Table 4.9).

	Number of symptoms at diagnosis							
	unknown	1	2	3	4	5	6	7
number of patients	11	0	41	65	98	80	17	5
	3%	0%	13%	21%	31%	25%	5%	2%

Table 4.9 Proportion of patients against number of symptoms

One other interesting finding resulted from an examination of the number of parameters measured before a diagnosis was made in each of the three related conditions (Table 4.10). These figures describe the number of different investigation modalities performed and the number positive for each of the three groups of Non-Specific Colitis, Ulcerative Colitis and Crohn's disease which were included in the small pilot study. These figures, perhaps surprisingly, show that Crohn's patients have fewer investigations performed than those with Ulcerative Colitis or Non-Specific Colitis and that the proportion of positive tests is less than that of Ulcerative Colitis.

Non-Specific Colitis

No. of parameters measured	total in group	No. of +ve measurements 1	2	3	4
1	1	1	-	-	-
2	2	2	-	-	-
3	11	8	1	2	-
4	34	25	3	6	-
total	48	36	4	8	0

Ulcerative Colitis

No of parameters measured	total in group	No. of +ve measurements 1	2	3	4
1	-	-	-	-	-
2	-	-	-	-	-
3	10	0	0	10	-
4	37	1	1	13	22
total	47	1	1	23	22

Crohn's Disease

No of parameters measured	total in group	No. of +ve measurements 1	2	3	4
1	-	-	-	-	-
2	10	0	10	-	-
3	11	1	1	9	-
4	29	0	8	8	13
total	50	1	19	17	13

Table 4.10 Positive findings at diagnosis

When the OMGE criteria were applied to the Crohn's group 91% were found to pass the criteria for Crohn's disease. This compares favourably with the large retrospective survey undertaken by the OMGE group. Actual scores of Crohn's patients varied widely with a range from 1 to 144 - the mean being 57.9 and the median being 59. This serial type of testing has prevented several individuals - 2 with vascular lesions in the bowel, 2 with endometriosis and 4 with post irradiation symptoms - from being incorrectly

admitted to the Register because they had symptoms of IBD and had Crohn's by OMGE criteria. Similarly using only the OMGE criteria other conditions such as acute ileitis, gastroenteritis or individuals with post gastric surgery symptoms may inadvertently have been classified as Crohn's or Ulcerative Colitis.

Summary

These results indicate that the retrospective survey based on inpatient statistics is a valid method for initial case capture on which to base the retrospective survey save for one major qualification. It must be appreciated that large numbers of false positives exist within this potential Crohn's group and that this whole group must subsequently be screened using a recognised scoring system to eradicate the large number of false positives. The validity of this method is further confirmed by the few patients who were picked up as sufferers of Crohn's disease from the primary care enquiry. Furthermore, support for this argument is also suggested by the small numbers of patients initially diagnosed as Non-Specific Colitis or Ulcerative Colitis following inpatient care and who were subsequently diagnosed as suffering from Crohn's disease.

Figures also indicate that the accuracy of the inpatient diagnostic coding for Crohn's disease has improved over the years and that Crohn's disease is still the most difficult of the related bowel inflammations to diagnose.

These findings suggest that the retrospective database contains an accurate and valid picture of Crohn's disease in Tayside between 1968-83.

CHAPTER 5

FINDINGS FROM THE REGISTER

5.1 INTRODUCTION

The following sections demonstrate the potential value of this type of computerised data collection where data is closely linked to powerful audit and analysis facilities. It has not been the intention to look in depth at one particular aspect of Crohn's disease but to take a broader view and attempt to demonstrate the advantages of this type of approach.

The various sections therefore show how an overview of a topic can be produced - the epidemiological aspects of the disease - and then how specific points gleaned from this overview can be investigated in greater detail - Crohns in the elderly and Crohn's in Arbroath. Other sections demonstrate how one particular aspect of the disease - the sections on pathology and radiology - can be systematically audited and then analysed in depth. The value of 'linked data' is also highlighted in for instance the treatment section - where data relating to surgery can be analysed in conjunction with for example pathogical or radiological findings.

By taking this approach the author hopes to have shown that this type of on-going data collection process can not only help further the understanding of the disease through audit and analysis but also provide a facility which has the potential to help in patient management.

5.2 EPIDEMIOLOGICAL ASPECTS OF CROHN'S DISEASE IN TAYSIDE

The analysis of the epidemiological aspects of the retrospective data collection is now presented. In order to smooth out any annual fluctuation in trends individuals on the Register have been grouped into those diagnosed within particular four year periods. Calculated trends have therefore been obtained from four such periods covering the years 1968 - 1983; those diagnosed before 1968 have not been included in these calculations because data collection is incomplete.

Incidence and Prevalence

Average annual age/sex specific and age/sex adjusted (using 1981 census figures for Tayside) incidence rates are shown for each interval from 1968 (Fig 5.1). Incidence has increased over each 4 year period though the rate of increase is perhaps slowing. This trend is generally reflected in each of the age bands examined although the increase appears to be maintained in the elderly population while in the 20-39 group there has been a considerable decrease in rate over the last 4 years studied. A similar picture is seen when incidence is related to sex. Incidence has increased in both males and females until 1980-83 when there has been a marked reduction in the rate seen in females in the 20-39 and 40-59 age groups while there has been a substantial increase in the elderly group; the rate for males has however increased across all age bands.

	1968-71	1972-75	1976-1979	1980-83
average annual incidence				
time of diagnosis	2.2	4.3	4.9	5.2
onset of symptoms	2.2	4.2	4.9	unknown
point prevalance	16	31	47	65

Table 5.1 Average Annual Incidence / Prevalence rates (per 100,000) 1968-83

Average Age/Sex specific incidence rates per 100,000 per year

	1968-1971 pop=397605 M=189413 F=208192		1972-1975 pop=401177 M=191621 F=209556		1976-1979 pop=400600 M=193658 F=207002		1980-1983 pop=396174 M=188728 F=207446	
	no.	rate	no.	rate	no.	rate	no.	rate
0-19								
All	4	.91	9	1.7	15	3.12	19	4.24
M	2	.90	3	1.15	5	2.02	9	3.94
F	2	.93	6	2.43	10	4.29	10	4.56
20-39								
All	29	7.14	34	8.54	41	9.50	34	7.82
M	14	7.07	12	6.00	13	5.89	20	9.17
F	15	7.28	22	11.11	28	13.26	14	6.47
40-59								
All	7	1.93	15	4.07	15	4.01	18	5.00
M	4	2.32	6	3.41	4	2.26	10	5.78
F	3	1.66	9	4.66	11	6.01	8	4.27
≥60								
All	1	.29	11	3.33	7	2.12	18	5.26
M	-	-	2	1.54	2	1.55	3	2.21
F	1	.44	9	4.49	5	2.49	15	7.25

Average Age/Sex adjusted incidence rates per 100,000 per year

	standard population	1968-71	1972-75	1976-79	1980-83
		"No." diagnosed in standard population			
0-19					
M	57090	1.57	2.01	3.54	6.90
F	54836	1.70	4.43	7.82	8.31
20-39					
M	54527	12.97	11.00	10.80	16.82
F	54090	13.46	20.53	24.51	11.96
40-59					
M	43240	5.36	7.89	5.27	13.37
F	46781	3.55	9.96	12.84	9.13
60+					
M	33871	-	4.55	4.58	6.52
F	51739	.85	8.68	4.81	14.01
	-----	----	----	----	----
	396174	39.46	69.05	74.17	87.02
age/sex adjusted rate		.99	1.74	1.87	2.20

Age/Sex incidence rates

Figure 5.1

Table 5.1 refers to incidence rates related both to time of diagnosis and to onset of symptoms using a standard population (396,000). The final value in the group where incidence is related to the onset of symptoms has been omitted because only 75% of those who develop symptoms within any 4 year period will in fact be diagnosed during this period (Table 5.2).

		Date symptom onset			
		68-71	72-75	76-79	80-83
Date	68-71	33			
of	72-75	8	51		
diagnosis	76-79	1	13	63	
	80-83	1	2	18	64

Table 5.2 Date of diagnosis & Date of symptom onset

Point prevalence rates (Table 5.1) have been calculated using the last day of each 4 year period to calculate the rate. Figures again show an increase in prevalence of the disease with no apparent slowing.

It has been suggested that a greater awareness on the part of clinicians has played a role in the increasing incidence of Crohn's disease. If this were the case the time from symptom onset to diagnosis might have been expected to fall during the period of study. No evidence could be found to support this hypothesis; Table 5.3 shows that there was no significant increase in the numbers diagnosed at less than 6 months from symptom onset nor indeed was there any indication of a downward trend in the time to diagnosis in the Crohn's population as a whole.

Most groups agree that there has been a genuine increase in incidence of the disease (Miller 1974, Bergman 1974) over the period under examination. However, it must be remembered that incidence rates might also alter through changes in diagnostic

fashion - the use of onset of symptoms as opposed to date of diagnosis, the introduction of more specific tests or new methods of investigation - such as endoscopic examination of the colon or indeed from changes in referral patterns or geographical boundaries.

	(in months)			
	1968-71	1972-75	1976-79	1980-83
< 6mths	50%	45%	56%	46%
6-11mths	14%	23%	14%	17%
≥12mths	36%	32%	30%	37%

Table 5.3 Time from Symptom Onset to Diagnosis

The frequency of cases by postcode (fig 5.2) taking the postcode of residence at the time of symptom onset has shown significant clustering in the Arbroath area of the region (DD11) over the 16 years under investigation ($p < .05$).

Age and sex of Crohn's population

Age at diagnosis (fig 5.3) shows the majority of patients with the disease are diagnosed between the ages of 20-39 with the mean age being 36.8 years, the median age 32 years and the mode 26 years. When trends reflecting the age at diagnosis were examined the most significant finding in the 16 year period (fig 5.4) was the rate of increase of diagnosis in the elderly 60 age group. In this group it rose from 2% of those diagnosed in 1968-71 to 25% of those diagnosed in 1980-83.

The sex ratio of Tayside's Crohn's population is M:F, 41:59. In comparison the sex ratio of the Tayside population as a whole is M:F 48:52 the difference between the populations does not however reach statistical significance. Figures for each 4 year period from 1968 are shown in Table 5.4 but once again just fail to demonstrate significant variation.

CROHN'S POPULATION BY POSTCODE
(Frequency per 1,000 population)

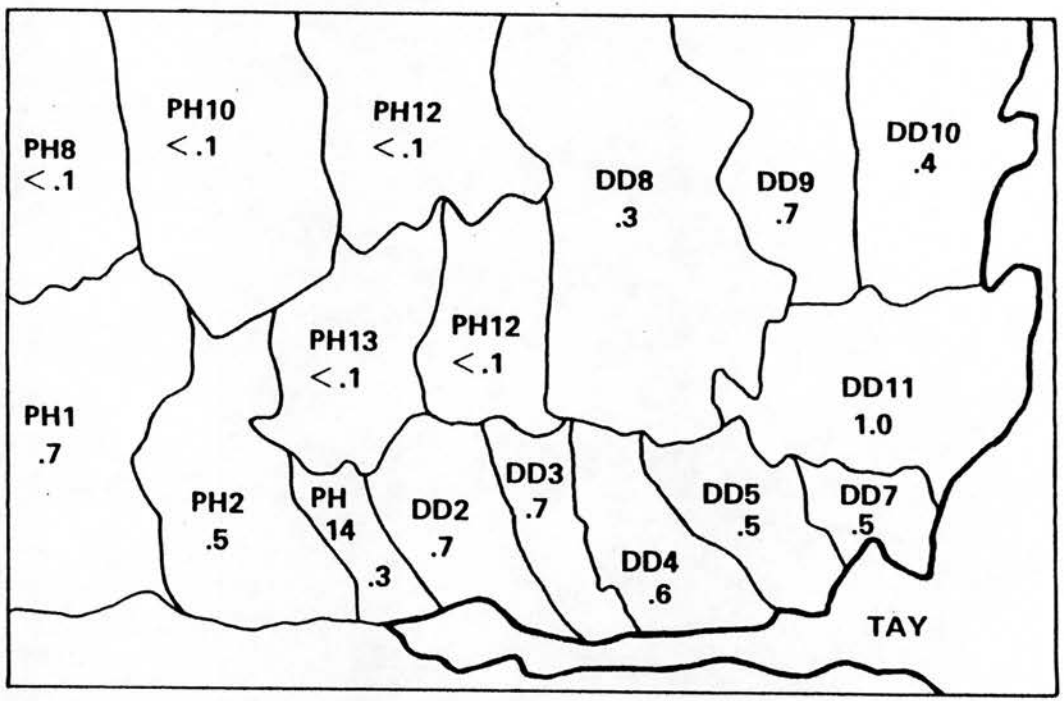


Figure 5.2

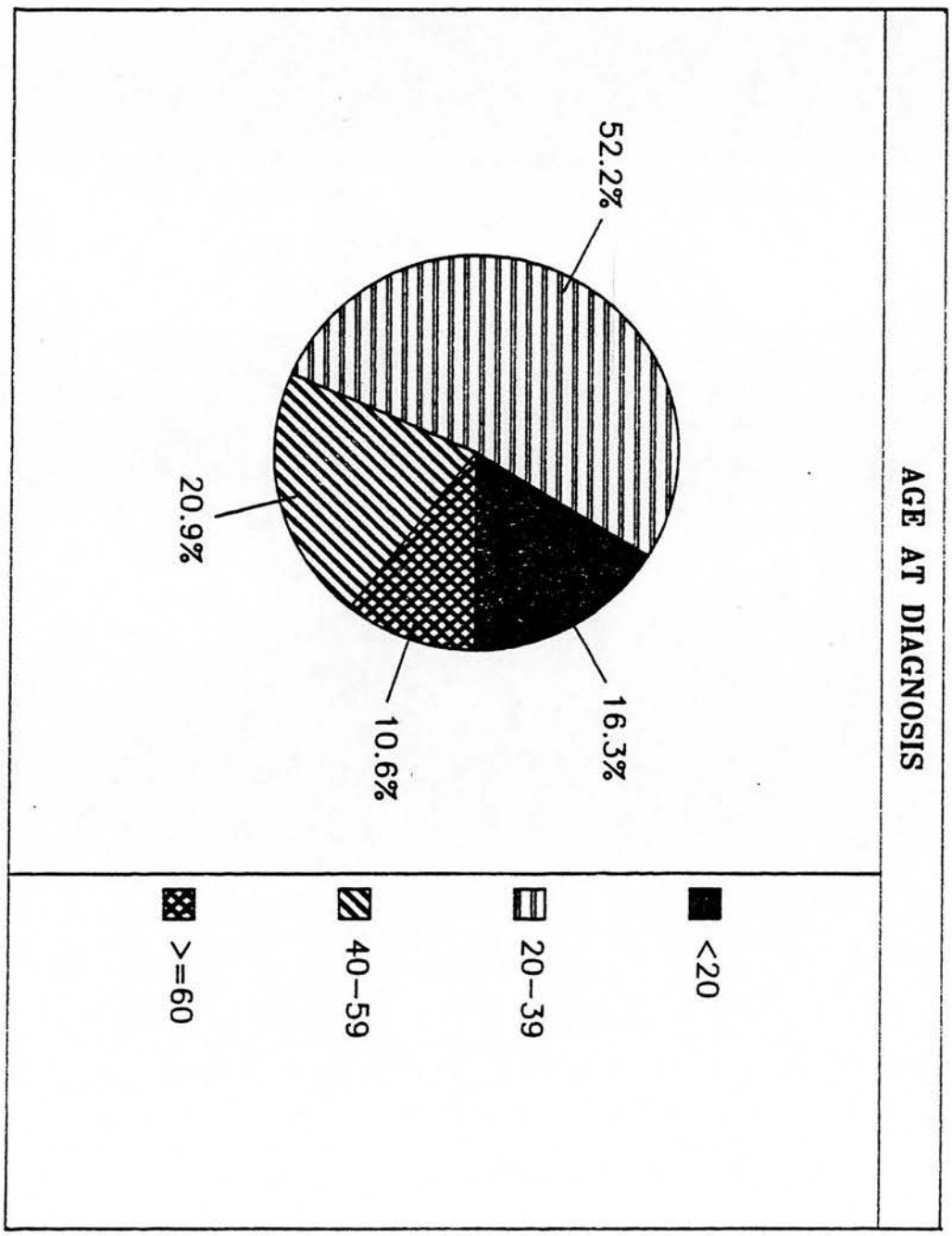


Figure 5.3

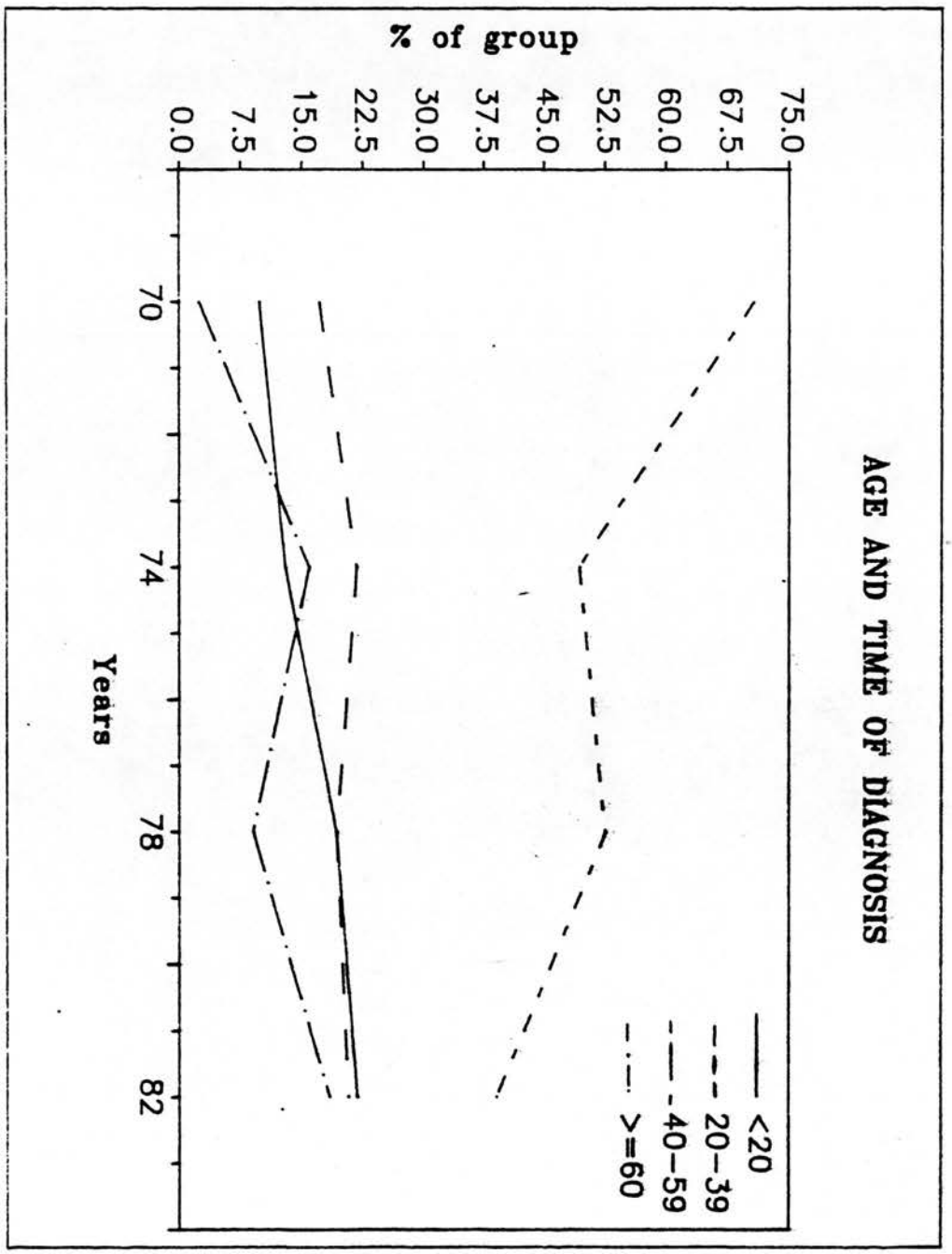

AGE AND TIME OF DIAGNOSIS
% of group
75.0
67.5
60.0
52.5
45.0
37.5
30.0
22.5
15.0
7.5
0.0
70
74
78
82
Years
<20
20-39
40-59
>=60

Figure 5.4

	pre 1968	68-71	72-75	76-79	80-83	total
Male	19	20	23	24	43	129
Female	22	21	46	54	46	189

Table 5.4 Sex and Date of Diagnosis pre 1968-83

Interestingly figures show that an initial equality in sex ratio was replaced in 1972-75 with a sudden increase in the proportion of females. This ratio was maintained until the 1980-83 period when the number of newly diagnosed males showed a marked increase almost equalising the ratio. Therefore although there remains a preponderance of females even for the 1980-83 period the most recent ratio suggests that the number of males is increasing more rapidly than that of females.

Furthermore the sex ratio by age at diagnosis shows a significant variation in the over 60 group where 79% were females (Table 5.5).

	<20	20-39	40-59	60 and over
% males	45	43	43	21
% females	55	57	57	79

Table 5.5 Sex and Age at diagnosis

An increase in the number of females is to be expected in the over 60 group (1981 census figures for Tayside's elderly population - 60 years or over - showed M:F 40:60). The differences between the 60 and over and the under 60 groups of Crohn's patients and between the elderly Crohn's cohort and those in the elderly general population were both significant ($p < .05$).

Site of disease

Changes have also occurred in the site of disease at diagnosis (Table 5.6). Although the frequency of both ileo-colic and small bowel disease has remained relatively constant over the 16 year period there has been a significant increase in large bowel disease ($p < .01$).

number of patients with disease in:-	small bowel	ileo-colic	large bowel	discon-tinuous
68-71	14	18	3	6
72-75	24	19	16	7
76-79	22	23	20	13
80-83	25	15	29	14
Total	85	75	68	40

Table 5.6 Site of Disease & Date of Diagnosis

When the site of disease at diagnosis was compared with the age at diagnosis (Table 5.7) the increase in large bowel disease was more evident in the over 60 age group. In this group 48% were classified as large bowel disease at diagnosis. One other interesting feature of this comparison was the relatively high proportion of the <20 group who had discontinuous or multiple sites of disease.

	(percentage in each group)			
	<20	20-39	40-59	60 & over
small bowel	17	32	35	36
ileo-colic	26	40	22	9
large bowel	23	13	33	48
discontinuous	32	13	3	3

Table 5.7 Site of Disease & Age at Diagnosis

Mode of presentation

The mode of presentation to the hospital service - either emergency/acute or as an out-patient - was collected for all those on the Register. Not surprisingly the majority of individuals initially presented to an out-patient clinic, however it was interesting that as many as 37% of patients initially presented as a hospital emergency prior to subsequent diagnosis. There was no age/sex variation in the mode of presentation of the disease.

Clinical features

Data on both presenting symptoms and their duration (Table 5.8) showed the most common symptom was abdominal pain (69%) closely followed by diarrhoea (64%) then weight loss (55%). Only 18% had rectal bleeding, 20% lassitude and 12% perianal symptoms. The majority of the 11 with mouth ulcers were in fact young children of whom several were directed to their doctor by their dentist. Of those with mouth ulcers at presentation 6 were diagnosed as discontinuous disease, 1 small bowel, 3 ileocolic and 1 large bowel disease. This finding tends to confirm that Crohn's disease may affect any part of the gastrointestinal tract and suggests that a field of change may exist or develop throughout the gastrointestinal tract in the disease.

Unfortunately it was not possible to determine the duration of some of the presenting symptoms.

A total of 51 (16%) of those on the Register also had associated symptoms on presentation, some indeed had several. Table 5.9 shows that 8% of those with Crohn's disease also had some form of arthropathy and 8% had a dermatological problem on presentation.

	time in months						
symptom	1	2-5	6-11	12-33	24-79	unknown	total %
	percentage of patients per period						
diarrhoea	14	38	15	11	9	13	64
abdominal pain	21	35	12	14	10	8	69
rectal bleeding	16	43	17	9	5	10	18
lassitude	11	58	12	6	6	7	20
weight loss	3	50	16	14	8	9	55
	Number of patients per period						
fistula	0	1	0	0	0	4	
anal symptoms	3	8	9	7	6	37	
mouth ulcers	0	5	2	1	2	11	
fever	4	2	0	0	0	6	
others	1	3	1	2	3	11	

Table 5.8 Presenting Symptoms and their Duration

Collection of information on past medical history showed 171 (54%) of those on the Register had some previous medical history while 111 (35%) had some previous gastrointestinal history. Small but notable numbers also had a past history of genitourinary, respiratory tract & musculoskeletal symptoms (Table 5.10).

Arthropathy	Eye problems	Liver disease	Skin problems	Other
26	7	3	27	1
8%	2%	1%	8%	-

Table 5.9 Associated Symptoms

Gastro-intestinal	Genito-urinary	Respiratory	Musculo-skeletal
111	24	23	19
35%	8%	8%	6%

Table 5.10 Past Medical History

At the time of diagnosis 29% were single, 61% married and 7% widowed, 12% lived alone, 77% lived in a family unit and only 5 lived in a communal dwelling. The majority (62%) of individuals lived in an urban environment while 38% lived in a rural area. Unfortunately it was not possible to obtain similar official figures for the Tayside population to permit a direct comparison to be made.

Within the Crohn's population 9 (2.8%) individuals were found to have a first degree relative with a history of Ulcerative Colitis (4) or Crohn's disease (5).

Smoking habits were obtained in 264 patients (83%) on the Register, 150 (57%) were identified as smokers while 11 (4%) had previously smoked. Information on alcohol intake was found in 241 (76%) of patients 70 (29%) of this group did not drink. Accurate figures for alcohol intake were not possible in this retrospective data collection exercise however the case records described 71% as being 'little' to 'moderate' drinkers.

The occupations of the Crohn's population is shown in Table 5.11. This system was developed as it was thought to be appropriate for Crohn's disease. Unfortunately the author was not aware at the start of this work of the availability of census figures relating to occupation which would have made comparison possible with the regional population.

unskilled	53	17%
skilled	39	12%
school/student	23	8%
clerical	42	13%
white collar/ professional	61	19%
homemaker	64	20%
unknown/other	37	11%

Table 5.11 Occupation

During the period under study 254 patients were diagnosed as suffering from Crohn's disease - 34 Crohn's patients died, however in this group only 11 died as a result of their Crohn's disease or a complication thereof. In June 1985 there were 255 patients living in Tayside with Crohn's disease 55% of whom were being followed up, 29% had been discharged and 21% lost to follow up. Figure 5.5 seeks to present survival and Life Table data on the Crohn's population and is based on the group diagnosed between 1964-1966 and diagnosed or dying within each subsequent two year period

Summary

Both incidence and prevalence of Crohn's disease in Tayside have increased steadily over the period of study. Clustering has been identified in one geographical area of the region. Although the majority of Crohn's patients are diagnosed when between 20-40 years of age an increasing number of elderly patients are also developing the disease. There have also been some variations in the sex ratio of the Crohn's population the most significant of which was the high proportion of females over 60 being diagnosed with the disease. Large bowel disease is becoming progressively more common particularly in the elderly patient.

Symptoms remain diverse, the most common being abdominal pain, weight loss and diarrhoea. Associated symptoms appear relatively uncommon although as many as 35% have a past history of gastrointestinal problems. A family history of inflammatory

Survivors in tabular format

nos. & date diagnosed	Survivors after 2 year periods								
	2	4	6	8	10	12	14	16	18
1966 11	11	10	10	10	10	9	8	7	7
1968 21	20	20	20	20	19	19	19	19	
1970 20	19	19	19	19	19	19	19		
1972 22	21	21	20	18	18	18			
1974 47	46	45	45	42	40				
1976 34	33	33	32	32					
1978 44	44	41	41						
1980 47	47	45							
1982 42	42								

LIFE TABLE

Years after	Ratio survivors	ratio dying	Number alive after each 2yrs/1000	Number dying after 2yr periods	cumulative ratio survivors
0	.98	.02	1000	20	.98
2	.97	.03	980	29	.95
4	.99	.01	951	9	.94
6	.96	.04	942	38	.90
8	.97	.03	904	27	.88
10	.98	.02	877	18	.85
12	.98	.02	859	17	.84
14	.96	.04	842	34	.81

Survival & Life table of Crohn's population based on initial diagnosis between 1964-1966

Figure 5.5

bowel disease is uncommon in the Tayside Crohn's population. Although the disease may carry a high morbidity, figures show that the mortality is relatively low.

5.3 CROHN'S IN THE ELDERLY

Several workers (Carr 1982, Fabricus 1982) have looked at Crohn's disease in the elderly patient and suggested that the disease shows different features from those found in younger patients. Early analysis of the Tayside Crohn's population tended to confirm this view and because this group has not been described as part of an epidemiological study it was felt that they merited further examination.

The population was first divided into two cohorts those under 60 years and those 60yrs and over at diagnosis. Data was analysed for each group independently then compared. This age division was chosen because it permitted comparison with other available data (Fabricus 1982).

Clinical findings

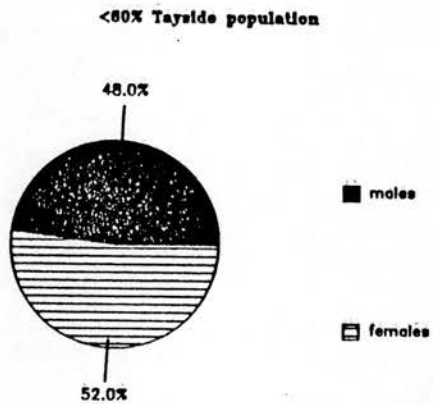
Of the 536 patients identified as possible Crohn's patients over the 16 year period only 318 fulfilled the register's diagnostic criteria for Crohn's disease. Of these 318 patients 35 were aged 60 or over at the time of diagnosis. The incidence of the disease (Table 5.12) in this elderly group has increased significantly over this period when compared with the younger group ($p < .01$). The figures have been obtained using a 'standard' population of 396,000.

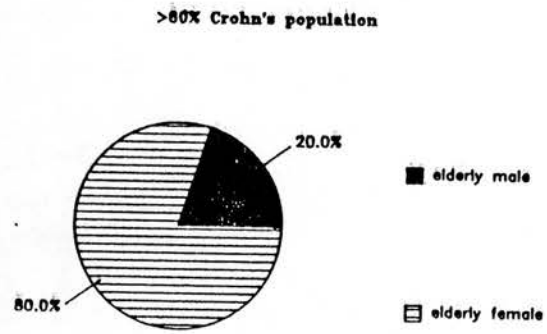
	68-71	72-75	76-79	80-83
Age at diagnosis				
≥60yrs	0.6	3.19	2.03	4.65
<60yrs	3.2	5.3	5.72	5.72

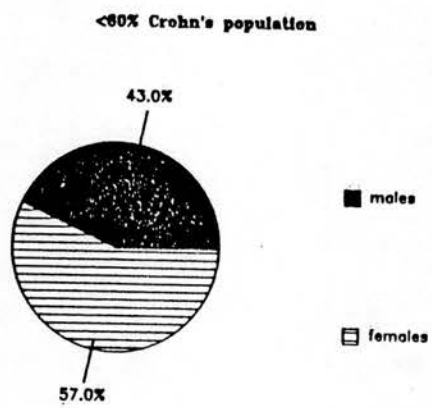
Table 5.12 Annual average Incidence rates (per 100,000)

The sex ratio shows a marked preponderance of females M:F ratio of 20:80 in the elderly group. The relative ratios are shown in fig 5.6.

CROHN'S AND THE ELDERLY – SEX RATIOS







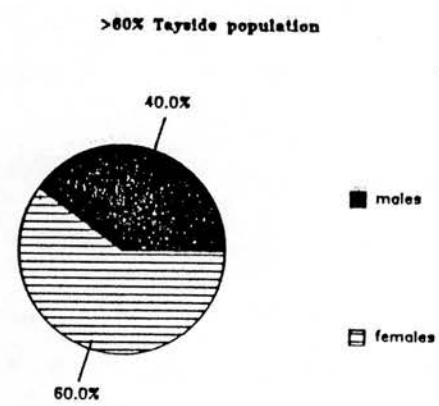


Figure 5.6

The difference between the groups reaches statistical significance ($p < .05$) when the elderly female group is compared with the younger female Crohn's group and also when compared with the over 60 years female Tayside population.

The differences in the site of disease at diagnosis are presented in Table 5.13 and show a large number of the elderly group with large bowel disease. These figures show that large bowel disease is significantly more common in the elderly group ($p < .001$).

	≥60 (n=35)		<60 (n=278)	
small bowel	12	34%	84	30%
ileocolic	4	11%	90	32%
large bowel	16	46%	54	19%
discontinuous	2	6%	40	14%

Table 5.13 Site of disease at diagnosis

The increasing incidence of large bowel disease is reflected in Table 5.14 which shows this increase as a percentage of those diagnosed in the elderly group compared to the younger group over the 16 year period. The Table also shows that large bowel disease in general is becoming more common.

	68-71		72-75		76-79		1980-83	
≥60 group	0/1		7/11	63%	2/7	29%	7/16	44%
<60 group	3/40	7%	9/58	16%	18/71	25%	22/71	31%

Table 5.14 Increasing frequency of large bowel disease

Data from the Register also showed that the mode of presentation to the hospital service was similar in both groups, 39% emergency and 61% via a clinic

appointment in the elderly and 41% and 59% in the younger group respectively. The time to diagnosis from onset of symptoms is shown in Table 5.15 and displays no significant variation between the groups.

	% in each group	
	<60	≥60
time to diagnosis		
<6mths	50.7	45.0
6-11mths	15.9	27.5
≥12mths	33.4	27.5

Table 5.15 Time to diagnosis from symptom onset

Despite similarities in the mode of presentation and time to diagnosis, symptoms were found to vary with abdominal pain being significantly more common in the elderly group ($p < .001$). Weight loss and rectal bleeding were also more common in the 60 and over group (Table 5.16) although the differences were not significant.

	≥60yrs n=35	%	<60yrs n=283	%
abdominal pain	21	60	49	18
weight loss	21	60	150	54
rectal bleeding	9	26	49	18
diarrhoea	22	63	179	64

Table 5.16 Presenting symptoms

Investigations

A histological diagnosis was obtained in 32 (91%) of the 60 and over cohort and 192 (69%) in the under 60 group ($p < .01$). Examination of the specific findings in each of the groups showed that the elderly patient was more likely to have evidence of

granuloma, transmural inflammation, giant cells and crypt abscesses than in the younger group (Table 5.17)

	≥60yrs n=35	%	<60yrs n=283	%
granuloma	21	60	135	60
transmural	12	34	72	26
giant cells	12	34	82	29
crypt abscess	7	20	43	15

Table 5.17 Histological findings

Comparison of the radiological investigations showed similar significant findings. Only 10 (29%) of the elderly group had radiological evidence of Crohn's disease while the younger group showed evidence of disease in 173 (63%) of individuals ($p < .01$). Interestingly, of the 10 elderly patients with radiological evidence of disease 7 had the diagnosis made on Barium enema and only 3 on Barium Meal & Follow-through. Furthermore of the 7 who had a diagnosis made on Barium enema 3 showed evidence of the disease in the terminal ileum.

Endoscopies carried out in each of the cohorts revealed that 80% of sigmoidoscopies in the elderly group demonstrated macroscopic inflammatory changes in the rectum (58% in the under 60 group). Conversely gastroscopic and colonoscopic examinations showed more evidence of macroscopic inflammatory changes in the younger group - 48% against 30% for gastroscopy and 60% against 55% for colonoscopy.

Certain haematological & biochemical parameters also varied at the time of diagnosis (Table 5.18).

	≥60yrs		<60yrs		
Hb <10gm/dl	7	n=31	39	n=231	p<.05
WCC >10,000	24	n=30	108	n=235	p<.001
Albumin <34gm/dl	18	n=24	95	n=195	p<.05
Protein <60gm/dl	14	n=24	49	n=203	p<.01

Table 5.18 Haem/Biochem findings at diagnosis

In the elderly group 20% had a Hb <10gm/dl against 14% in the younger group. There were significant differences in white cell count, albumin and protein levels at the time of diagnosis even taking into account the normal reduction in both albumin and protein levels in the aged patient.

Treatment

Surgical treatment was more common in the younger group, 401 operations being performed (1.4 operations per patient) against 35 in the elderly group (1.0 operations per patient). 8 patients (23%) in the elderly group and 65 (24%) in the under 60 group did not require surgery.

Overall, 17 (48%) of the elderly group had either a small bowel resection or right hemicolectomy (168 (59%) in the under 60 group). Although large bowel disease was more common in the elderly group the percentage requiring operation was no different from that in the younger group with large bowel disease.

Only 3 (9%) of the 60 and over group required further surgery while 122 (43%) of the younger patients had at least two operations ($p < .001$). In the younger group 80 had a second operation within 3 years of diagnosis.

The most common reasons for operation are shown in Table 5.19 - note many individuals had more than one reason for operation.

	≥60yrs n=27	%	<60yrs n=219	%	
obstruction	8	14	73	11	
abdo mass	9	15	37	6	p<.05
peritonitis	6	10	71	11	
failed medical Rx	3	5	97	15	p<.01
unknown diagnosis	20	33	101	15	p<.01

Table 5.19 Reason for operation

Accurate retrospective data collection on medical management was hard to obtain therefore notes were only kept on the types of medical treatment each individual had received at some point in their management. Table 5.20 shows the more common forms of medical treatment given in each group. Figures revealed that fewer of the elderly required medical treatment and fewer were given steroids or salazopyrin. Although treatment varied in each age group the differences between the age groups did not reach statistical significance except for treatment with salazopyrin.

These findings perhaps suggest that Crohn's disease in the elderly patient is less aggressive in nature and requires less treatment than in the younger patient. However, they could also suggest that clinicians felt that treatment was in fact less effective or the side effects too great to merit a trial in this elderly group.

	≥60yrs n=35	%	<60yrs n=283	%	
no medical Rx	8	23	32	12	
steroids	16	57	177	64	
salazopyrin	12	34	158	57	p<.05
azothiaprine	4	11	52	19	

Table 5.20 Medical treatment in both age groups

Outcome

During the period under study 11 of the elderly patients and 23 of the younger group died. However of those deaths only 5 in the elderly and 6 in the younger group were directly attributable to Crohn's disease.

Summary

Comparison of the elderly and younger Crohn's patients shows a significant variation between the groups and suggests that in Tayside the rate of increase in incidence in the elderly group is higher than that in the under 60 group. The elderly Crohn's patient is more likely to be a female with large bowel disease. Large bowel disease was found in almost half of the elderly patients diagnosed between 1980 and 1983.

Differences also occur between the groups in symptoms, radiological, pathological, endoscopic and haematological / biochemical investigations, treatment and reason for operation. The findings suggest that the disease is perhaps less aggressive and the morbidity less than in the younger group.

5.4 CROHN'S IN ARBROATH

For several years it had been the clinical impression of several clinicians in the region that the incidence and prevalence of Crohn's disease was high in the Arbroath area. Using postcode of residence at onset of symptoms it was found that there was a significant difference in the frequency of proven Crohn's disease in the postcode area of DD11 (Arbroath area) when compared with numbers resident in postcode areas throughout the rest of the district during the period under examination (fig 5.2). This apparent increase in frequency or 'clustering' has, as far as can be determined, not been described previously. Miller's group (Miller 1975, Miller 1976) attempted, without success, to identify 'time - space clustering' in Crohn's populations in their quest to confirm an aetiological link with transmissible infective agents. Evaluation has been understandably difficult because of the relatively small number of cases involved in an area making it difficult to prove or disprove the existence of this phenomenon.

It was felt that this apparent clustering merited closer evaluation. The Arbroath group was selected and epidemiological information obtained and compared with the overall Crohn's population.

The total number of individuals being diagnosed as having Crohn's disease has increased rapidly over the past few years (Table 5.21).

		number diagnosed				
	Av.pop	60-67	68-71	72-75	76-79	80-83
Arbroath	21494	4	2	0	5	11
Tayside (exc.Arbroath)	372506	29	39	69	74	76

Table 5.21 Frequency of diagnosis

Average annual age/sex adjusted incidence rates, using 1981 census figures for Tayside, have been calculated from this data for each 4 year period under investigation (Table 5.22). These figures confirm that there has been a significant increase in incidence over this period ($p < .01$) when compared to the rest the Crohn's population of Tayside.

	1968-71	1972-75	1976-79	1980-83
	Age / sex specific rates for Arbroath			
20				
M	--	--	10.98	5.48
F	--	--	--	5.88
20-39				
M	7.02	--	6.66	25.90
F	7.27	--	6.84	6.64
40-59				
M	--	--	8.72	17.49
F	--	--	--	8.00
60				
M	--	--	--	--
F	--	--	--	15.00
	----	----	----	----
	3.57	--	8.30	17.35
	no. diagnosed in standard population (in Fig 5.1)			
	26.31	--	64.24	126.88
	age/sex adjusted rates in standard population			
Arbroath	.66	--	1.62	3.20
Tayside	.99	1.74	1.87	2.20

Table 5.22 Average Annual age/sex adjusted incidence rates per 100,000

The figures show in particular a significant increase in incidence over the 1980-83 period. Similar figures are obtained if onset of symptoms is used to calculate the incidence (Table 5.22)

The sex ratio has been calculated (fig 5.7) and perhaps surprisingly shows significant variation from that of the overall Crohn's population ($p < .05$).

In order to determine whether this variation in sex ratio is of recent origin the sex ratio has been calculated for periods from 1960-67 and then each 4 year period thereafter (Table 5.23).

	60-67	68-71	72-75	76-79	80-83
Arbroath Males	2	1	0	4	7
Tayside (ex Arbroath)	17	19	23	20	35
Arbroath Females	2	1	0	1	4
Tayside (ex Arbroath)	20	20	46	53	41

Table 5.23 Changes in Sex ratio 1960-83

Although the total numbers of patients in the Arbroath area is small making statistical analysis less clear there is a notable difference in the M/F ratio in the Arbroath area over the last 8 years.

Ages at diagnosis have been calculated and compared within each group (Table 5.24) and show that although more of the Arbroath group are under 20 at diagnosis the differences do not reach statistical significance.

SEX RATIO BY POSTCODE

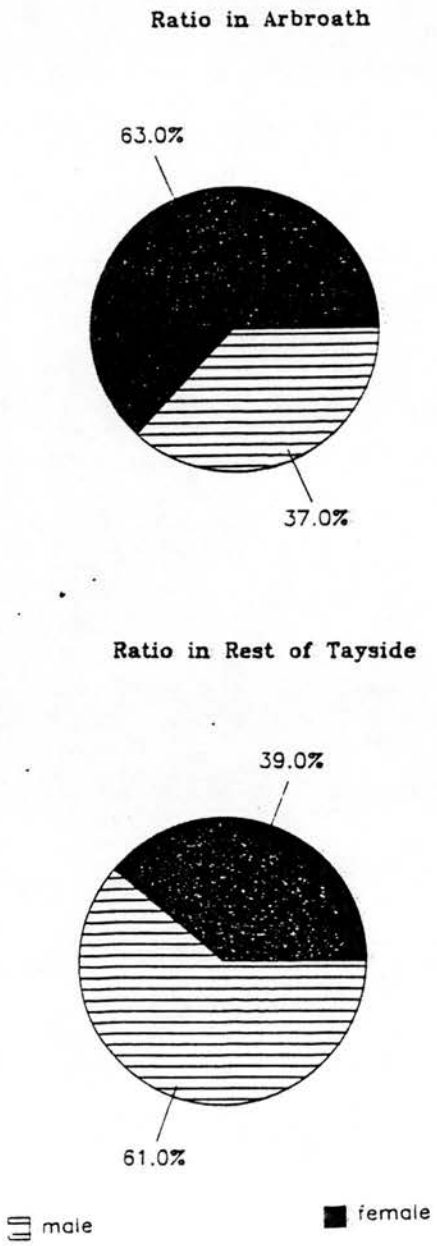


Figure 5.7

Age	Arbroath		Tayside (except Arbroath)	
<20	6	27%	46	16%
20-39	11	50%	150	52%
40-59	4	18%	61	21%
≥60	2	9%	33	11%
unknown	1		8	

Table 5.24 Age at diagnosis

When the under 20 group was looked at more closely, 4 (17%) were found to be school children at the time of symptom onset while in the rest of Tayside only 14 (5%) individuals developed symptoms as school children ($p < .01$).

Site of disease at diagnosis is shown in (Table 5.25) - the difference between these groups is not significant.

	Arbroath		Tayside (except Arbroath)	
Small Bowel	8	33%	89	31%
Ileo-colic	5	21%	89	31%
Large Bowel	7	29%	64	25%
Discontinuous	3	12%	41	14%

Table 5.25 Site of disease at diagnosis

There was no significant difference between the mode of presentation nor the time to diagnosis between the groups however as one would expect in a younger population a higher percentage were still single at diagnosis. There was no difference in severity of disease at diagnosis as observed from comparison of the diagnostic score index - Arbroath patients (65 median, 55 mean), Tayside patients (59 median, 57 mean). Patients with the disease in the Arbroath area had similar numbers of radiological investigations and operative procedures carried out suggesting that there was no

difference in the method of investigation of this group nor did the disease appear to be more aggressive in nature.

Summary

The Arbroath Crohn's population is similar in many respects to the rest of Tayside's Crohn's population however there are significant differences in incidence rates, sex ratio and age at onset of symptoms over the past 8 years which merit further investigation. Figures show that the age / sex distribution of the Arbroath population is similar to that for the rest of Tayside suggesting that direct population comparison is valid. The cause of this apparent variation remains unclear. There appears to be no obvious variation in the method of investigation or management with patients either being referred to Ninewells or Stracathro Hospital for medical or surgical consultation. No single consultant is therefore involved in investigating this group of individuals. Several points and possible associations have however been observed and are worthy of note.

Arbroath is famous for its fish in particular the 'Arbroath smokey' - literature review demonstrates similar areas of high incidence in coastal areas Cardiff and Upsalla - (Maybury 1979, Bergman 1975) where a high intake of seafood is also likely.

Of more interest perhaps is the observation that the Arbroath area is the only area in Tayside that does not draw any of its water supply from the main water purification plant which serves most of Dundee and Angus districts. These points will be discussed further in a subsequent section of this thesis.

5.5 THE RADIOLOGY OF CROHN'S DISEASE IN TAYSIDE

5.5.1 Radiological Audit

The 318 patients on the register had a total of 1,010 radiological or isotope investigations performed between 1960 and early 1985. This figure does not include plain abdominal or chest radiographs. The overall breakdown of investigations is given in Table 5.26 which shows that barium meal and follow-through was the most common investigation performed closely followed by barium enema.

Type	Nos Invest	Normal	(%)	Abnormal	Unknown
Barium meal & F-T	419	101	(24%)	312	6
Barium enema	363	120	(33%)	240	3
Small Bowel enema	64	25	(39%)	44	0
Barium meal	31	18	(58%)	10	0
Biliary investigation	8	23	(82%)	5	0
Intravenous pylogram	50	31	(62%)	19	0
Ultrasound	19	15	(78%)	4	0
others	86	--	--	--	

Table 5.26 Investigations

These figures show that even in the Crohn's population there are large numbers of normal radiological investigations - 31% of all investigations in the Crohn's group were reported as normal. More specifically 76% of the barium meal and follow-through and 67% of the barium enema examinations demonstrated some abnormality. Surprisingly in view of other reports (Truelove 1981, Keddie 1982) the small bowel enema demonstrated fewer abnormalities than either of the other primary bowel investigations with only 61% showing some evidence of disease. This may reflect a more careful selection of patients for this investigation for instance only for those individuals who have had negative barium meal and follow-through and barium enema investigations but yet have clinical evidence of disease.

Figures also demonstrate the relative increased risk of urinary tract problems in those with Crohn's disease. Fifty Intravenous pylograms performed in 46 patients gave a positive return in 19 investigations.

Of the 877 specific barium investigations (Table 5.27) performed, 416 were considered to demonstrate evidence of Crohn's disease - that is 47% (416/877) of all the bowel investigations performed and 69% (416/606) of those showing some abnormality.

Type	Abnormal	Inflamm changes	Crohn's disease	Ulcer colitis	Non-Spec colitis	Other
Barium meal	10	0	4	0	0	6
Barium meal & FT	312	32	253	0	0	27
Barium enema	240	38	121	26	2	55
Small Bowel enema	44	3	38	1	0	2
	----	---	---	---	---	---
	total 606	73	416	27	2	90

Total number barium studies 877

Table 5.27 Findings from barium studies

Of those investigations labelled as Crohn's disease 61% were obtained from barium meal and follow through, 29% barium enema, 9% from small bowel enema and 1% from barium meal.

The relative diagnostic return for each type of investigation performed within the region (Table 5.28) reveals that barium meal and follow through gives the best diagnostic return (60%) followed closely by the small bowel enema (55%). Barium enema investigations give a significantly poorer return (33%) in comparison with the small bowel investigations ($p < .001$).

Type	total	+ve	%
Barium meal & F.T.	419	253	60
Small Bowel enema	69	38	55
Barium enema	363	121	33

Table 5.28 Diagnostic return

The average number of barium investigations per patient on the register is 2.75, the range being from 0-7. Each patient had a diagnosis of Crohn's disease made on 1.3 occasions.

Trends have been calculated for both type, and findings of the primary bowel investigations performed on the Crohn's population during the period under study (Table 5.29).

	Number of patients per group					
Type	60-63	64-67	68-71	72-75	76-79	80-83
Barium meal & F T	9	19	52	95	130	77
Barium enema	4	12	58	72	89	98
Small Bowel enema	0	0	2	5	6	42
	--	--	---	---	---	---
totals	13	31	112	172	225	217
Radiological Diagnosis						
Normal	3	3	21	57	101	128
Crohn's	6	17	60	92	109	86
Other inflam	4	9	21	15	23	23
no. newly diag Crohn's cases	15	18	41	69	79	87
ratio normal/ abnormal x-ray	.23	.1	.2	.35	.43	.54
ratio normal/ Crohn's diagnos	.5	.18	.35	.62	.92	1.5
number x-rays/ registered patient	.86	.94	1.5	1.2	1.00	.68

Table 5.29 Trends in barium studies

These figures suggest an increasing frequency of investigation as the prevalence of the disease has increased or indeed that as the number of investigations increases so the number diagnosed as Crohn's disease increases. However, it must be remembered that these figures only deal with patients with a confirmed diagnosis of Crohn's disease and do not take into account all the investigations performed on patients whom it was thought might have had the disease. The fall in the number of barium meal and follow-through examinations has probably resulted, at least in part, from the increasing use of the small bowel enema examination.

Of more interest perhaps in these days of financial constraint is the increasing number of investigations performed on the Crohn's population which are reported as demonstrating no abnormality (fig 5.8). This is coupled with a rapidly increasing ratio of normal investigations to those reported as demonstrating evidence of Crohn's disease (fig 5.8). One could suggest that these figures represent a waste of resources and speculate that the ratios are due to an increasing awareness of the disease, the ease by which tests can be arranged or a reduction in clinical acumen. However one could also argue that the free availability of such radiological investigations results in a better service to the patient even though it may not be cost effective. Similarly in some patients a negative investigation may in fact be a very positive finding - for instance by preventing surgical intervention.

5.5.2 Radiology in the diagnosis of Crohn's disease

Of the 317 patients on the Register 270 (85%) had a specific radiological examination for investigation of their Crohn's disease. In this group 211 (78% of those having x-ray examinations) had some evidence suggesting inflammatory bowel disease. Of the 270 undergoing radiological examination, 189 (70%) were described as having a radiological diagnosis of Crohn's at some point in their disease however only 156 patients

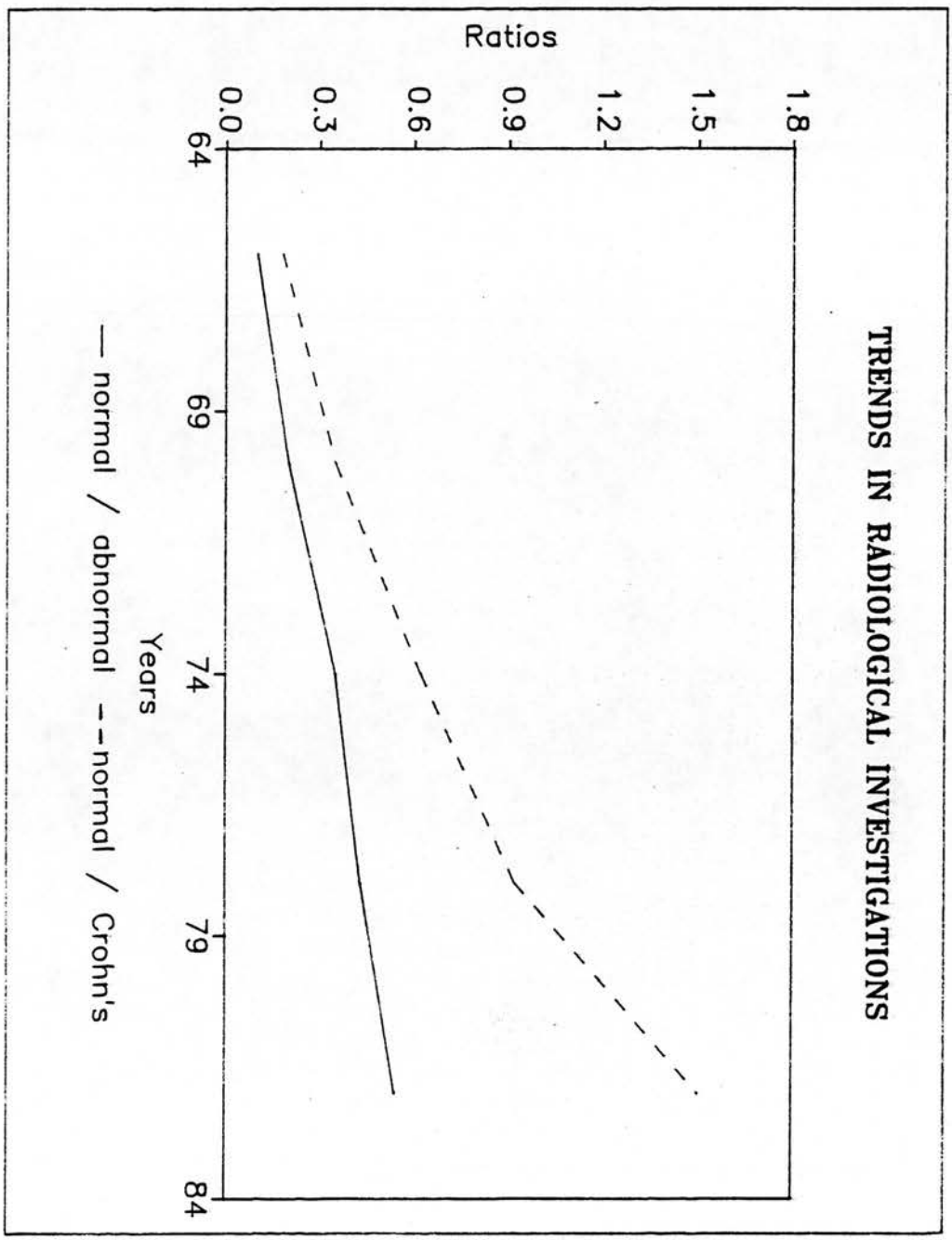

TRENDS IN RADIOLOGICAL INVESTIGATIONS
Ratios
1.8
1.5
1.2
0.9
0.6
0.3
0.0
64
69
74
79
84
Years
— normal / abnormal --normal / Crohn's

Figure 5.8

(58%) were shown to have a proven radiological diagnosis when they were initially diagnosed. This section has described a simple audit of investigations performed. The figures do not take into account observer variation between radiologists which may well be considerable, indeed, this point perhaps merits further clarification as the Register moves into the prospective phase.

The number of patients with positive barium studies is shown in Table 5.30 along with the number who had a positive radiological diagnosis at the time of diagnosis. Figures also show that 63% of those having barium meal and follow-through, 42% having barium enema and 55% having small bowel enemas revealed changes sufficient to merit a diagnosis of Crohn's disease at some point in their disease.

Type	Number invest	Crohn's patients	%	No. with Crohn's at diagnosis	%
Barium meal & F-T	232	147	63	116	50
Barium enema	233	96	42	65	28
Small Bowel enema	62	34	55	13	21
Barium meal	29	2	7	0	

Table 5.30 Patients with a radiological diagnosis of Crohn's disease

This suggests that in Tayside the barium meal and follow through gives the best diagnostic return in those shown to have a radiological diagnosis of Crohn's disease followed closely by small bowel enema and then barium enema.

In each of the investigations which were reported as abnormal a note was kept of the sites deemed abnormal. The gastrointestinal tract was split into oesophagus, stomach, duodenum, jejunum, ileum, terminal ileum, caecum, ascending, transverse, descending and sigmoid colon, rectum and anal canal. Examination of the sites of bowel involvement in these barium studies showed that although the barium meal and follow-through and small bowel enema are used primarily to identify small bowel disease a significant proportion of those demonstrating disease were also reported as showing

abnormalities in the large bowel - 96 out of the 516 (19%) of sites defined as abnormal were in large bowel. Similarly barium enemas showed evidence of small bowel disease in 87 of the 397 sites shown to be abnormal on barium enema study (22%).

The most common radiological findings reported from each type of investigation (Table 5.31) showed that 'disease', 'irregularity' of the mucosa, 'narrowing', 'dilatation', 'ulceration' and 'stricture' to be the most frequently described abnormalities.

	Frequency of Finding			
Finding	Barium Meal & F-T	Barium enema	Small bowel enema	Total
narrowing	104 32%	55 23%	9 20%	168 28%
obstruction	12	6	3	21 3%
dilatation	70 22%	9 <1%	3 7%	84 14%
diverticulum	5	24 10%	2	31 5%
mass	14	3	0	17 3%
reduce function		36	25	63 10%
fistula	27	21	2	50 8%
polyps	6	10	1	17 3%
ulcers	39 12%	51 21%	4 9%	94 16%
stricture	43 13%	24 10%	5 11%	72 12%
skipareas	19	8	4	33 5%
thickwalls	15	5	5	25 4%
cobblestoning	10	3	2	15 2%
irregularity	90 28%	80 33%	7 16%	177 29%
disease	105 33%	74 31%	15 34%	194 32%
Total abnormal investigations	318	240	44	602

Table 5.31 Radiological findings from barium studies

In those investigations which showed some abnormality the most common findings were 'disease' (32% of abnormal x-rays), 'irregular mucosa' (29%), and 'narrowing of the lumen' (28%). Other common findings were the presence of 'ulcers', 'dilatation' (14%) and 'stricture formation' (12%). Barium meal and follow-through examinations revealed narrowing and/or disease and/or irregularity on the mucosa for 1 in 3 of abnormal investigations and although definite obstruction was only present in 4% of the reported findings dilatation was found in 22% of follow-through procedures. Barium

enema examinations demonstrated slightly more 'ulcers' (21%) and a lower incidence of 'narrowing' (23%) than in the follow-through procedures.

Despite being well recognised radiological features the frequency of 'skip areas', 'fistula', 'thick walls' and 'cobblestoning' was surprisingly low - each being present in less than 10% of abnormal investigations.

5.5.3 Clinical Radiological Aspects in the Crohn's Population

Closer scrutiny of the 189 patients with radiological diagnosis of Crohn's disease showed some variation between groups. When the population was grouped by age at diagnosis (Table 5.32) 73% of the 20-39 group were found to have radiological evidence of Crohn's disease while in the elderly group only 29% had radiological evidence of disease.

There was no variation in sex ratio with 60% of each sex showing radiological features of Crohn's disease. Nor was there any significant variation in radiological diagnosis in patients presenting with different symptoms although those presenting with pain gave a slightly higher (67%), and those with PR bleeding (48%) a slightly lower rate of positive radiological investigation.

Whether a radiological diagnosis was obtained did however depend on the site of disease at diagnosis. Whilst only 25% of patients with large bowel disease at diagnosis showed radiological evidence of disease, the figures for small bowel, ileocolic and discontinuous disease were 67%, 74% and 72% respectively. This difference is highly significant ($p < .001$) when those with large bowel disease are compared with the other sites of disease.

	number	Radiological diagnosis	% total
Age group			
<20	52	29	56
20-39	161	117	73
40-59	65	30	46
≥60	35	10	29
Sex			
Male	129	76	59
Female	189	113	60
Symptoms			
diarrhoea	203	123	60
pain	220	148	67
wt loss	173	104	60
PR bleeding	50	24	48
Site of disease			
smallbowel	97	65	67
ileocolic	94	70	74
large bowel	71	18	25
discontinuous	44	32	72

Table 5.32 Clinical radiological features

Summary

Radiological enquiry has shown that although less than half of those on the Register had a radiological diagnosis of Crohn's disease before diagnosis almost 80% of those having a barium study showed radiological evidence of disease at some point in their disease. In Tayside the barium meal and follow-through still provides the best positive return of all the barium studies performed.

Although the number of radiological investigations, particularly of small bowel enemas has increased in parallel with the Crohn's population, an ever increasing number of these investigations are proving to be normal which may relate to poorer patient selection or over-investigation. It was also noted that one third of all barium studies in the Crohn's population were reported as normal.

Both age at diagnosis and site of disease appear to influence the frequency of radiological diagnosis. Finally, in Tayside, narrowing and irregular mucosa are the most commonly reported abnormalities from barium studies in patients with Crohn's disease.

5.6 THE PATHOLOGY OF CROHN'S DISEASE IN TAYSIDE

5.6.1 Pathology Audit

A total of 688 specimens from the registered Crohn's population were submitted for examination to the Pathology departments in Tayside. Only information on specimens directly or indirectly related to the patients' Crohn's disease was entered into the Register. Of the total, 401 were biopsies and were subjected to microscopic examination only, while 287 gross specimens underwent both macro and microscopic examination. The findings in 350 were sufficient to merit a diagnosis of Crohn's disease. The increasing number of specimens demonstrating features of Crohn's disease is shown in Fig 5.9. The rate of increase has however slowed over the past 4 years. Only prospective study will show if this trend is to continue.

Figures also reflect the increasing frequency and importance of endoscopic procedures as a source of specimens for examination with proportionately many more biopsies being obtained over recent years (Fig 5.10).

The majority of gross specimens submitted were either ileum (66%) and/or right colon (44%). Other samples submitted for examination included transverse colon (15%), left colon (17%), rectum (11%), anal canal (6%) and jejunum (3%).

The most commonly reported macroscopic findings were thick wall, reported in 93% of gross specimens, and ulcerated mucosa which was evident in 98% of specimens examined. Other common features were lymphadenopathy and narrowing/stricture formation present in 46% of gross samples while serosal injection and thickened submucosa were found in 38% of specimens respectively. Less common findings were thickened mesentry, fistula and skip areas.

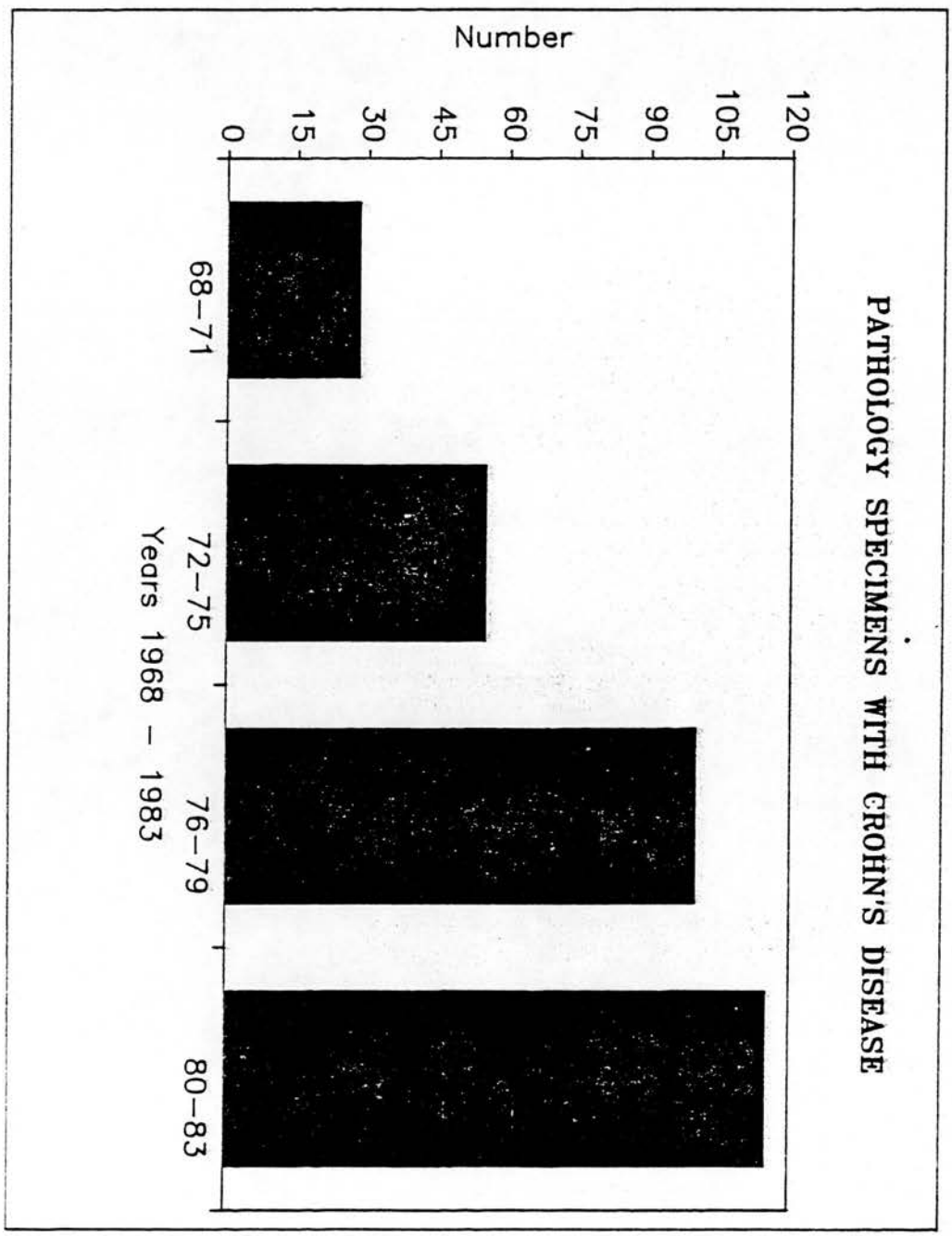

PATHOLOGY SPECIMENS WITH CROHN'S DISEASE
Number
0
15
30
45
60
75
90
105
120
68–71
72–75
76–79
80–83
Years 1968 – 1983

Figure 5.9

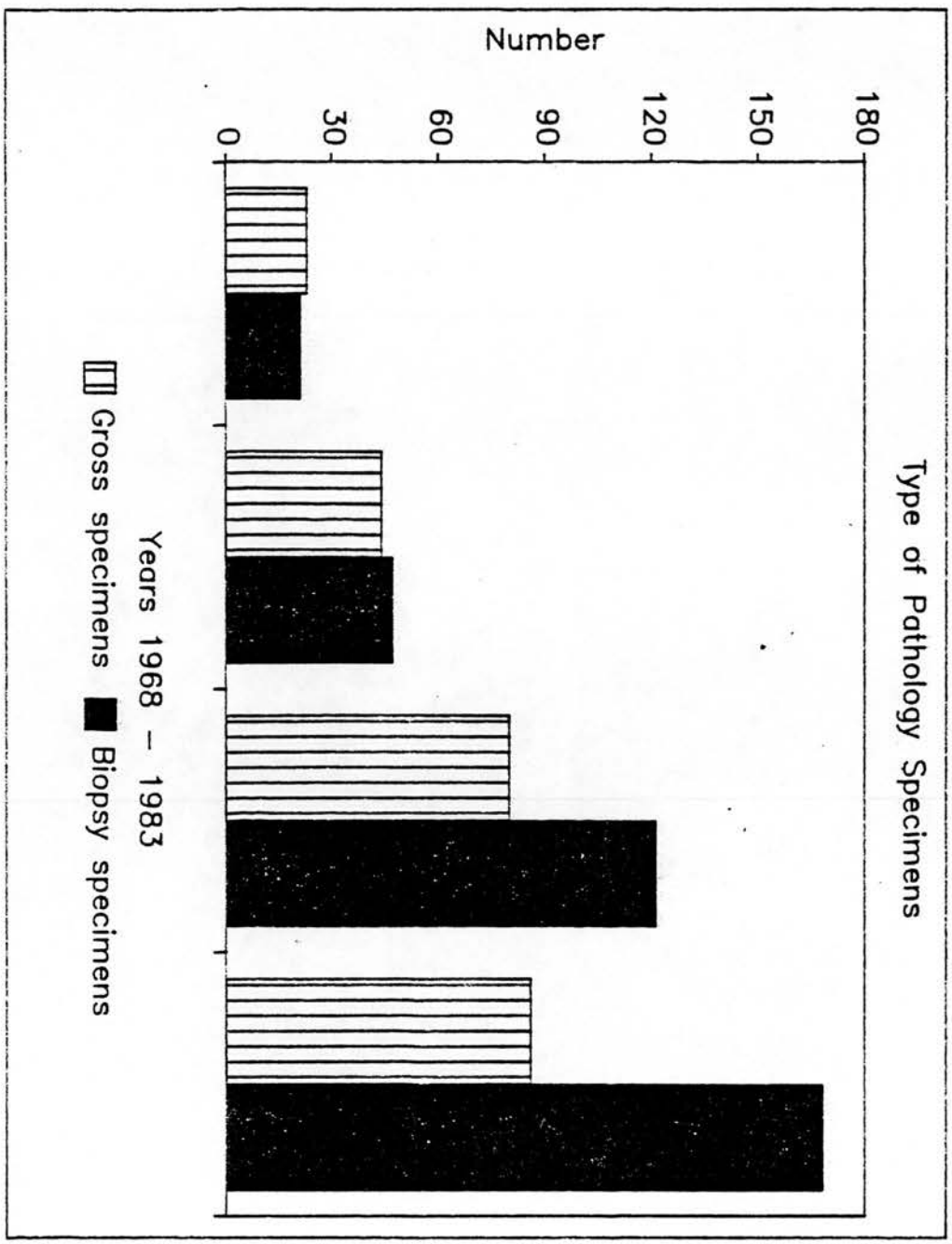

Number
0
30
60
90
120
150
180
Type of Pathology Specimens
Years 1968 - 1983
Gross specimens
Biopsy specimens

Figure 5.10

Audit of microscopic examination demonstrated 252 (37%) instances of rectal tissue, 180 (26%) of the terminal ileum, with the right and left colon being reported in 16% and 14% respectively. All other areas of bowel were described in less than 6% of specimens examined. The most commonly reported microscopic findings were chronic inflammatory changes, granuloma formation, acute inflammation, giant cells and transmural inflammation (Table 5.33). Other recognised features were plasma cells/macrophages/eosinophils (11%), fibrosis (7%), reactive hyperplasia (11%), reduction in goblet cells (6%), and crypt abscesses (9%).

	number	%
chronic inflammation	424	62
acute inflammation	217	32
granuloma	231	34
giant cells	118	17
transmural inflammation	102	15

Table 5.33 Microscopic Findings

5.6.2 Clinical Pathology

A total of 280 of the 318 registered patients (88%) had at least one specimen submitted for examination. Of this group 226 (81%) were found to have a pathological diagnosis of Crohn's disease. A pathological diagnosis was therefore obtained in 71% of those on the Register. Of this group 172 (76%) had a diagnosis based on at least one gross macroscopic specimen while the remainder (54) had the diagnosis based on simple biopsy and microscopic examination.

Table 5.34 shows some of the findings from the clinical pathological enquiry.

	number with crohn's	number with pathology diagnosis and %	
sex			
males	129	93	73
females	189	132	70
age groups			
<20	52	39	75
20-39	161	105	65
40-59	65	48	73
≥60	35	32	91
site of disease			
small bowel	97	49	51
ileocolic	94	76	81
large bowel	71	59	83
discontinuous	44	35	80
duration of symptoms			
<6mths	174	126	72
6-11mths	43	36	83
≥12mths	80	56	70
symptoms			
rectal bleeding	58	54	93
wt loss	173	127	73
pain	220	156	71
diarrhoea	203	155	76

Table 5.34 Clinical Pathological Findings

Equal numbers of males and females demonstrated a positive pathological diagnosis.

When the population was split by age 91% of the 60 and over population showed a histological diagnosis of Crohn's disease while 75%, 65% and 73% of the under 20, 20-39 and 40-59 groups respectively had pathological evidence of the disease. The difference between the elderly and the rest of the Crohn's population was significant ($p < .01$).

The frequency of pathological diagnosis also varied with the site of disease. Those with small bowel disease demonstrated a pathological diagnosis on significantly fewer occasions than those with other sites of disease ($p < .001$).

When the duration of symptoms before diagnosis was examined it was found that individuals with symptoms for 6-11 months had positive histology in 83% of cases whereas those with symptoms for less than 6 months and a year or more had positive histological evidence of disease in 72% and 70% respectively. The presence of rectal bleeding as a presenting symptom was a good indicator that a pathological diagnosis would be obtained with 93% of those with this symptom demonstrating at least one positive biopsy showing Crohn's disease. The frequencies of pathological diagnosis in those presenting with diarrhoea, pain or weight loss as one of their symptoms were similar.

These figures suggest that the patient most likely to reveal pathological evidence of disease is one who, at the time of diagnosis, is over 60, with symptoms for 6-11 months - one of which is rectal bleeding - and who is thought to have large bowel disease.

5.6.3 Histological Findings

The microscopic findings of those with pathological evidence of disease were examined closely (Table 5.35). The four most common microscopic findings have been taken and compared with sex, site of disease and age at diagnosis. Results show that both site of disease and age at diagnosis vary with the histological findings. Several points were noted. Those with small bowel disease had a scarcity of microscopic findings compared to those with other disease sites. Granulomas became progressively more common in the distal bowel. Patients with discontinuous disease more commonly had evidence of granuloma formation than in the other groups. Microscopic findings also varied with age at diagnosis with granuloma formation being more common in the groups aged under 20 and 60 years and over at diagnosis.

	% of each group with finding			
	gran uloma	trans mural	giant cell	crypt absc
pathology diagnosis (226)	69	38	42	22
specimens submitted (280)	56	30	33	18
Sex				
male	53	27	26	20
female	47	26	32	13
Site of disease				
small bowel	26	22	14	3
ileocolic	55	35	36	10
large bowel	63	18	38	8
discontinuous	66	36	43	14
Age at diagnosis				
<20	65	25	33	19
20-39	43	25	30	12
40-59	48	29	25	20
≥60	60	34	34	20

Table 5.35 Histological Findings

Further interesting facts emerged when the sites of biopsies and microscopic findings were compared with the actual site of disease (Table 5.36). Figures demonstrate that in those with small bowel disease chronic inflammatory changes occurred in 39% of rectal/anal canal biopsies. Granuloma were however not found in any of these biopsies. Furthermore, in ileocolic disease a greater number of ano-rectal biopsies revealed microscopic changes - 31 (51%) showing chronic inflammatory changes and 14 (23%) demonstrating granuloma formation. As one would expect in discontinuous disease histological changes occurred throughout the gastrointestinal tract.

Microscopic changes in the upper gastrointestinal tract in those with large bowel disease were less common with only 3 of the 9 reported gastroscopy biopsy specimens showing evidence of chronic inflammation. This however still represents a relatively high positive return in those with large bowel disease.

These findings confirm the importance of endoscopic biopsy, particularly of the rectum, when investigating a patient thought to have Crohn's disease. The findings also lend support to the view that in Crohn's disease a field of change exists throughout the gastrointestinal tract.

The following is a key to Table 5.36 which demonstrates the microscopic findings by site of disease.

Key to table 5.36

D = duodenum	J = jejunum
I = Ileum	TI = terminal ileum
RC = right colon	TC = transverse colon
LC = left colon	R = rectum
A = anal canal	

Frequency of finding

The 97 patients had 41 microscopic reports relating to rectal or anal canal biopsies

Small bowel disease

	D	J	I	TI	RC	TC	LC	R	A
chron inflam	3	8	5	32	8	2	3	16	0
giant cell	0	2	2	9	3	0	0	0	0
<goblet cell	0	0	0	0	0	1	0	2	0
crypt absc	0	0	1	0	0	1	0	1	0
transmural	0	0	2	20	3	0	0	0	0
granuloma	1	2	4	22	4	0	0	0	0

Ileocolic disease

The 94 patients had 60 microscopic reports relating to rectal or anal canal biopsies

chron inflam	4	3	7	57	42	10	10	24	7
giant cell	0	0	3	25	18	3	1	4	5
<goblet cell	0	0	0	0	0	0	0	5	2
crypt absc	0	0	0	7	8	2	2	3	0
transmural	1	1	3	30	25	5	3	1	1
granuloma	0	3	6	43	33	4	1	10	4

Large bowel disease

The 77 patients had 9 biopsy reports relating to the stomach or duodenum

chron inflam	1	2	1	4	8	13	37	78	7
giant cell	0	0	0	0	3	5	13	15	3
<goblet cell	0	0	0	1	2	3	11	22	1
crypt absc	0	0	0	1	3	4	10	27	2
transmural	0	0	1	0	3	7	5	5	1
granuloma	0	0	1	0	5	10	21	37	5

Discontinuous disease

44 patients had 21 biopsy reports relating to stomach and duodenum and 63 relating to rectum and anal canal

chron inflam	9	3	4	24	18	7	23	38	7
giant cell	0	0	1	11	6	3	4	10	2
<goblet cell	0	0	0	0	0	0	0	4	1
crypt absc	0	0	0	1	2	2	3	3	0
transmural	1	2	3	12	5	2	1	3	2
granuloma	1	1	5	18	15	5	13	18	5

Table 5.36 Microscopic findings by site of disease

5.6.4 Granuloma in Crohn's disease

A closer examination was made of those with histological evidence of granuloma formation.

Pathological evidence of disease was, as previously described, most common in those presenting with symptoms of 6-11 months duration. Similarly and perhaps not surprisingly granulomas were also found more frequently in this group (28/42 - 66%) when compared with those with symptoms for <6months (84/174 - 48%) and for 12months (41/80 - 51%) prior to diagnosis.

Those found to have granuloma formation were grouped by sex and then compared with the site of disease at diagnosis and by age at diagnosis. Results showed considerable variation between the groups (Table 5.37).

	Males n=68 with granuloma		Females n=88	
Site of disease				
small bowel	19	28%	7	8%
ileocolic	23	34%	30	34%
large bowel	12	17%	34	39%
discontinuous	14	21%	15	17%
Age at diagnosis				
<20	17	25%	17	19%
20-39	33	48%	37	42%
40-59	14	21%	17	19%
≥60	4	6%	17	19%

Table 5.37 Variation in Granuloma formation

Although there is no significant overall variation in the ratio of males (68/129 - 53%) and females (88/189 - 47%) with granuloma, when each group was looked at more carefully it was noted that there was a significant difference in the sex ratios of those with granuloma when compared with the site of disease at diagnosis. When a similar comparison was made with the age at diagnosis the 60 and over female population was found to have a much higher proportion of their overall population with granuloma than

in the 60 and over male population; perhaps a reflection of the percentage of elderly women with large bowel disease.

The presence of granuloma in a patient with symptoms of inflammatory bowel disease has been recognised to be a good indicator of Crohn's disease. The frequency of granuloma per specimen was calculated as a measure of the liklihood of a pathology specimen in a Crohn's patient demonstrating a granuloma. Calculations showed that 49% of gross specimens submitted were found to contain granuloma and that the figure for biopsy specimens was much lower at 21%. These figures suggest that even in a patient being found to have or known to have Crohn's disease only 1 in 2 of macroscopic specimens and 1 in 5 biopsy specimens will demonstrate granuloma.

The prognostic significance of granuloma formation was examined by comparing those with and without granuloma with the rate of re-operation and present Register status. The number of operations required in each group is shown in Table 5.38 which shows that those found to have granulomas have more operations than those without evidence of granuloma formation.

	n	1		2		3		4	
with granuloma	157	124	79%	62	39%	33	26%	6	4%
without granuloma	160	99	62%	43	26%	10	6%	2	1%

Table 5.38 Number of Operations

One could argue that it is the operation itself which provides the macroscopic specimen from which a granuloma was found. However when the numbers requiring re-operation were examined in each group (Table 5.39) those with granuloma were not only found to have a greater probability of having an initial operation but also of having further operations after the first and subsequent procedures. The figures show that over 50% of those who have one operation will have a second procedure and 50% of this group will go on to have a third operation.

	operation number							
	1st		2nd		3rd		4th	
granuloma								
with	124/157	79%	62/124	50%	33/62	53%	6/33	18%
without	99/160	69%	43/99	43%	10/43	23%	2/10	20%

Table 5.39 Percentages requiring further operation

Further figures show that 54% of those known to have granuloma formation are being 'followed up' (38% in those without granuloma) and that 39% of those with granuloma have been 'discharged' or 'lost to follow-up' (47% in those without granuloma). Mortality statistics showed that of those who died during the study period (34) exactly half were noted to have shown granuloma formation.

These findings therefore suggest that the discovery of granuloma in a pathology specimen increases the morbidity firstly by increasing the likelihood of one or more surgical procedures being performed and secondly by increasing the likelihood of hospital follow-up.

Summary

In summary this section has shown that the increasing numbers of positive histological reports parallels the increase in incidence of disease and has demonstrated the increasing importance of endoscopic procedures as a means of obtaining specimens for histological examination.

Results also show that age, symptoms plus their duration and site of disease affect the pathological findings. Importantly a sizeable number of histological abnormalities can be found at sites distant to confirmed areas of disease.

Interesting facts have emerged in the group found to have granuloma formation, the most important of which is the suggestion that those with granuloma have a greater morbidity than those without granuloma.

5.7 ENDOSCOPY IN CROHN'S DISEASE

A full retrospective audit of endoscopy procedures was impossible because the documentation of procedures was often incomplete. Only those investigations which had been well documented were collected and subsequently analysed. Data relating to type and date of procedure, sites examined, findings and suggested diagnosis was collected and entered in the Register. Table 5.40 shows the number of procedures logged with the Register and the number of individuals who have undergone that particular investigation.

Type of endoscopy	total	% biopsied	number of patients	% of total Crohn's pop
gastroscopy	94	56	74	24
sigmoidoscopy	229	77	159	50
colonoscopy	84	76	64	20

Table 5.40 Endoscopy procedures

Despite a careful search of case records for evidence of endoscopy procedures only 50% of individuals had fully documented evidence of a sigmoidoscopy, 20% a colonoscopy and 24% a gastroscopy.

A total of 190 (60%) of the Crohn's population were identified as having had either a colonoscopy or sigmoidoscopy performed at some stage in their disease. The features of large bowel endoscopy were very non-specific with narrowing or stricturing only being noted in 21 (6%), polyps/pseudopolyps in 8 (2%), granular mucosa in 5 (1%) and cobblestoning in 2 occasions. The total number of auditable findings from large bowel endoscopy was 342. Figures also reflect the small number of endoscopies which were considered to demonstrate sufficient features to merit an endoscopic diagnosis of

Crohn's. A diagnosis was documented in 219 of the reported endoscopies, however in only 40 (18%) was the diagnosis of Crohn's disease made.

Endoscopic findings were graded 0, +, ++, or +++ of inflammation. Table 5.41 describes an audit of all those with at least '+' of inflammation. Of the 159 individuals who had a sigmoidoscopy 98 (62%) were noted to have inflammatory changes on at least one occasion while 52 (32%) never had any evidence of inflammatory changes.

	number patients	number with inflamm	% with changes
sigmoidoscopy	159	98	62
colonoscopy	64	38	60
gastroscopy	74	34	46

Table 5.41 Inflammatory changes on endoscopy

Similarly 38 (60%) of those individuals having a colonoscopy had evidence of inflammatory changes in some part of the large bowel. Interestingly of those with inflammatory changes on sigmoidoscopy, 15% had small bowel disease and 15% had ileocolic disease while in those with evidence of inflammation at colonoscopy 10% had small bowel disease and 15% ileocolic disease (Table 5.42). Furthermore 30% of those with colonoscopic and 19% of those with sigmoidoscopic evidence of inflammatory changes had discontinuous disease.

	positive sigmoidoscopy n=98	positive colonoscopy n=38
small bowel	15 (15%)	4 (10%)
ileocolic	15 (15%)	6 (15%)
large bowel	47 (48%)	16 (42%)
discontinuous	19 (19%)	12 (30%)

Table 5.42 Endoscopy - changes & site of disease

Of the 74 individuals having a gastroscopy 34 had inflammatory changes - 35% of this group had discontinuous disease, a higher proportion than might be expected with only 13% of the overall population having discontinuous disease.

Of the 190 individuals undergoing a large bowel endoscopic procedure 124 (65%) were found to have at least one occasion when inflammatory changes were observed. In this group only 39% (38/97) with a Crohn's diagnosis on barium enema showed evidence of inflammatory changes on endoscopy.

Of the 226 individuals with a confirmed pathological diagnosis of Crohn's 98 were from the group of 124 with evidence of large bowel changes on endoscopy. Similarly of the 189 with a confirmed radiological diagnosis of Crohn's disease, only 62 were from the group with inflammatory changes on large bowel endoscopy. Therefore only 43% and 33% of those with confirmed pathological and radiological changes respectively were shown at some stage to have endoscopic changes in the large bowel.

Endoscopic changes in the large bowel did not vary with sex or age at diagnosis however those presenting with diarrhoea, rectal bleeding, pain or weight loss had evidence of large bowel endoscopic changes in 50%, 90%, 30% and 35% respectively.

Summary

Although the retrospective endoscopy audit was incomplete it was noted that 65% of individuals having large bowel endoscopies performed showed evidence of inflammatory changes at some stage in their disease. Though the changes noted were often non-specific a significant proportion of those with small bowel disease were found to have large bowel endoscopic changes. This confirms the importance of these investigations particularly if rectal bleeding or diarrhoea are presenting symptoms.

Pathological and radiological evidence of disease are both relatively poor indicators of the likely presence of inflammatory changes at endoscopy.

5.8 HAEMATOLOGICAL & BIOCHEMICAL FINDINGS

The retrospective collection of haematological and biochemical data was a tedious task. Both Angus and Dundee district have had computerised biochemical laboratory systems since the early 1970's making time related collection of biochemical data possible for the majority of those on the register.

There were two aspects to this data collection:-

1. Results which relate to parameters at the time of diagnosis.
2. Results collected over a period of time following the diagnosis.

An attempt was made to generate a full haematological and biochemical profile at the time of diagnosis thus permitting analysis at this time. The initial results were then supplemented as the disease progressed from further investigations reported and subsequently filed in the case record. Where several values existed for a specific period the most abnormal result was collected - repeat investigations often related to periods of increased disease activity or hospital admission.

Results are therefore presented in terms of values at diagnosis followed by results appearing at some point in the patient's disease. Finally groups with abnormal results were looked at more closely to see if there were any associations with age, sex, site of disease and time to diagnosis.

5.8.1 Values at diagnosis or soon after diagnosis

The most commonly performed haematological and biochemical investigations are displayed in Table 5.43.

		abnormal	number performed	%
ESR	>10mmhr	74	102	72
Hb	<10gm/dl	12	273	4
WCC	>10,000/cc^3	127	269	47
Urea	<2.9umol/l	108	270	40
Bilirubin	>17mmol/l	10	209	5
Alk Phos	>120iu	23	218	11
GGT	>42iu	32	115	28
Protein	<60gms/l	65	231	28
Albumin	<34gms/l	103	223	46

Table 5.43 Abnormal haematological / biochemical tests at diagnosis

The table shows that the ESR, WCC, urea and albumin are all commonly abnormal at the time of diagnosis. Perhaps surprisingly only a few individuals had haemoglobin values of < 10gm/dl at diagnosis. Similarly a total of 53 of those on the Register (17%) had either a raised bilirubin, alkaline phosphatase or GGT at diagnosis.

Folate, vitamin B12, iron and TIBC measurements were also collected and analysed if the measurement had been made within 6 months of diagnosis (Table 5.44).

	abnormal	number performed	%
Folate (4-20μgm/ml)	67	111	60
B12 (230-800μgm/ml)	10	109	9
Iron (9-27mmol/ml)	71	94	78
TIBC (250-410μgmdl)	43	98	44

Table 5.44 Abnormal vitamin & iron at diagnosis

These figures demonstrate that even at diagnosis a not insignificant number of individuals already have low folate and iron levels.

Table 5.45 demonstrates the potential of the computer system's numerical analysis routines. Means, medians, modes and standard deviations have been calculated for commonly performed investigations at the time of diagnosis (Table 5.45).

	points	mean	median	standard deviation
Hb	273	12.25	12.00	1.808
WCC	269	10.03	9.00	3.878
ESR	107	38.93	33.00	26.460
Albumin	224	34.52	34.00	6.683
Protein	231	64.77	66.00	8.717
Urea	270	4.23	3.30	3.512

Table 5.45 Haem/biochem statistics at diagnosis

Similar calculations have been made for these parameters measured over the period following diagnosis (Table 5.46).

	points	mean	median	standard deviation
Hb	201	2.60	13.00	1.760
WCC	200	9.47	9.00	3.763
ESR	46	25.17	16.50	24.194
Albumin	203	36.37	37.00	6.414
Protein	205	62.85	64.00	9.035
Urea	200	4.75	3.90	4.307

Table 5.46 Haem/biochem statistics post diagnosis

Comparison of these parameters shows that the post diagnosis values show no significant variation from the values at diagnosis.

5.8.2 Abnormal values during the period of disease

Further analysis of all haematological / biochemical investigations held on the Register (Table 5.47) revealed that as few as 20 individuals had a recorded

haemoglobin value of less than 10gm/dl. Similarly a total of 169 individuals had WCC $>10{,}000cc^3$, 92 a protein level <60gm/l, 127 an albumin of <34gm/l and 145 a urea of <3mmol/l at some point in the disease. Abnormal LFT's remained uncommon over the course of the disease with only 80 (25%) being found to have an abnormal liver related parameter at some point during their disease.

	no. of patients with measurement	number abnormal	%
Haemoglobin	273	20	7
WCC	269	169	63
Protein	231	92	40
Albumin	223	127	57
Urea	270	145	54

Table 5.47 Abnormal haem/biochem at any time

5.8.3 Associations between Haematological / Biochemical parameters

Protein, albumin, white cell count and urea values were the most frequently abnormal haematological/biochemical parameters at the time of diagnosis. Each parameter was examined more closely to see if abnormal values varied with sex, age, site of disease and time to diagnosis (Table 5.48).

Results show that abnormal WCC, urea, protein and albumin values do not vary with the sex of the individual.

Figures for age at diagnosis, time to diagnosis and site of disease are displayed in Table 5.48. As one might expect the elderly patient's serum albumin and protein levels were below the normal range in up to 40% of individuals at the time of diagnosis - also notable is the large discrepancy between the number of under 20's with low protein (19%) and the number with low albumin (40%). Perhaps surprisingly the percentages of individuals with low protein or albumin levels did not appear to vary with the time taken to diagnosis. Those with small bowel and discontinuous disease more

commonly had reduced protein and/or albumin levels although the differences were not significant.

	Number of patients & % with:-							
	WCC		Protein		Albumin		Urea	
	>10000		<60gm/dl		<34gm/dl		<3mmol/l	
age at diagnosis								
<20 (52)	14	27%	10	19%	24	46%	19	37%
20-39 (161)	69	43%	19	12%	37	23%	67	42%
40-59 (65)	25	38%	20	31%	24	37%	14	22%
≥60 (35)	17	49%	14	40%	16	35%	6	17%
Site of Disease								
Small bowel (97)	43	44%	27	25%	36	37%	30	31%
Ileocolic (94)	41	44%	14	15%	24	26%	40	43%
Large bowel (71)	30	42%	14	20%	23	32%	20	28%
Discontinuous (44)	13	30%	8	20%	19	44%	18	41%
time to diagnosis								
<6mths	83/156	53%	34/130	20%	62/127	49%	59/174	34%
6-11mths	22/38	58%	9/32	28%	12/29	41%	19/42	33%
≥12mths	32/60	55%	17/56	30%	23/55	42%	29/80	36%

Table 5.48 Abnormal haem/biochem associations

Although WCC was raised in just under 50% of individuals at diagnosis there was no variation in age, time to diagnosis or site of disease in this group.

A low urea value was not associated with the site of disease although individuals with discontinuous or ileocolic disease demonstrated a slightly higher percentage with a urea <3mmol/l. Similarly the length of time to diagnosis did not appear to vary with the urea level at diagnosis however there were significant differences between those diagnosed at less than 40 years of age and those 40 years or over ($p < .001$).

Summary

Although few individuals were found to have abnormal haemoglobin values either at diagnosis or subsequently, many were shown to have low protein and albumin values even at diagnosis. Furthermore a relatively high proportion of patients also had

low iron and folate at diagnosis. Information on follow-up data suggests that there is no obvious continued and / or permanent deterioration in the recorded parameters as the disease progresses.

There were no significant clinical associations when the abnormal haematological and biochemical values were compared with age, sex, site of disease or time to diagnosis.

5.9 TREATMENT

From the retrospective survey it was impossible to determine accurate information on the medical treatment regimens of the Crohn's population. It was however possible by careful scrutiny of the patient records to identify many of the different types of medication that individuals had been treated with during the period of their disease. This, it was hoped, would create a baseline which could be developed more accurately in the prospective phase of the Register. The extraction of this data also revealed the difficulties associated with the retrospective collection of this type of information.

The documentation of operative procedures performed on each individual was more complete, therefore information on the date, reason for and type of operation was collected for each procedure performed. The analysis of this data was therefore more accurate. All procedures performed under general anaesthetic were audited except those described as an examination under anaesthetic.

5.9.1 Operative findings

A total of 455 operations were performed on 243 of the Registers' patients (77%) - that is 1.9 operations per patient having an operation, or 1.4 operations per registered individual.

The number of operations performed per patient is shown in fig 5.11. This figure shows that in the Crohn's population 23% had no operation at the time of the survey. Of the patients having an operation 54% had a second operation, 49% of this group had a third operation while a further 24% had a fourth procedure. At the time of the survey 77% of individuals on the Register had had one operation, 40% had two and 20% three operations.

Of the operations performed right hemicolectomy was the most common (Table 5.49).

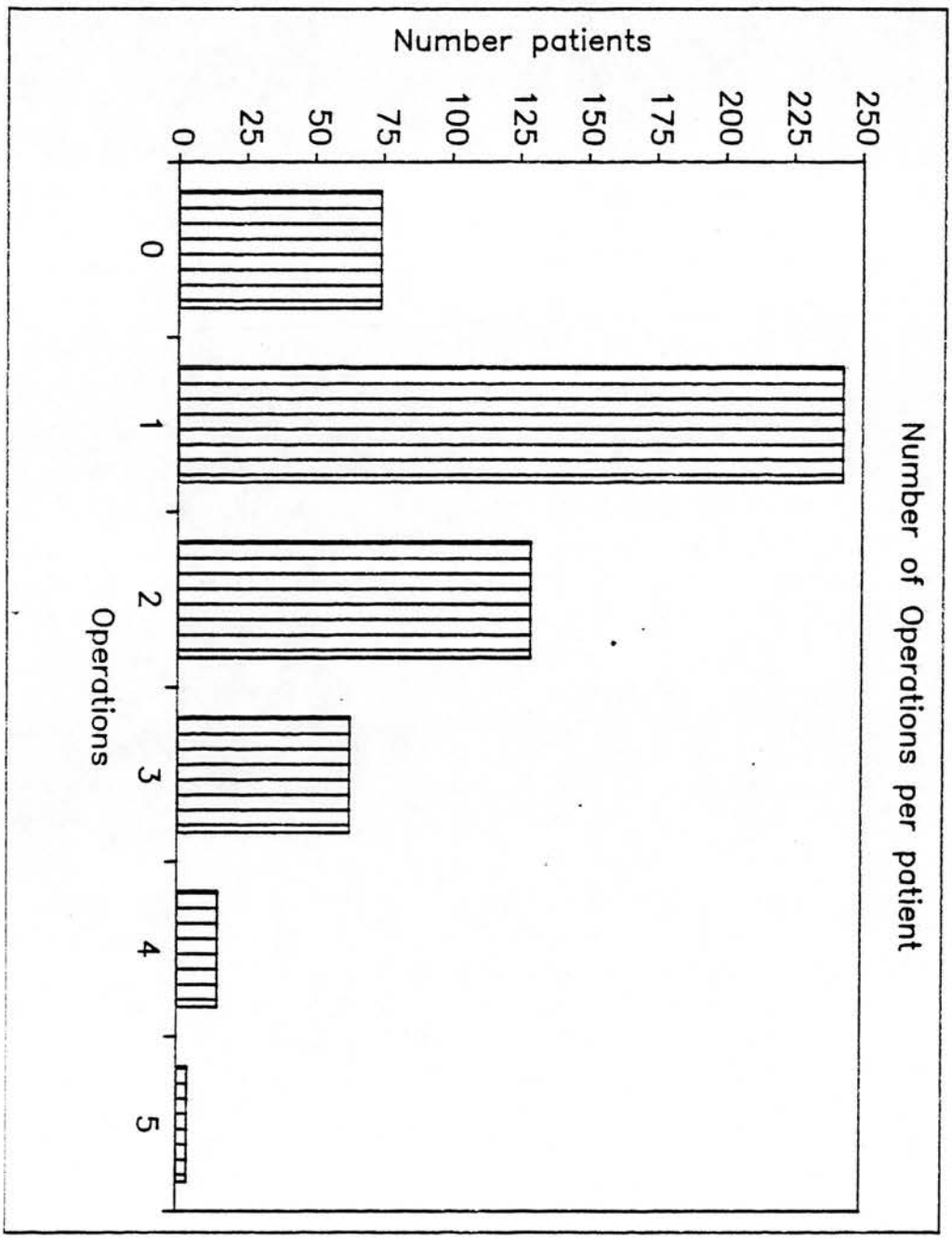

Number patients
0
25
50
75
100
125
150
175
200
225
250
Operations
0
1
2
3
4
5
Number of Operations per patient

Figure 5.11

	number
Rt hemicolectomy	112
small bowel resection	68
laparotomy	58
Lt hemicolectomy	11
transverse colectomy	3
colectomy	30
proctectomy	17
resection of ileum	14
panproctocolectomy	11
colostomy	25
ileostomy	11
bypass operation	11
re-anastomosis	6
drain abscess	26
excision fistula	14
division adhesions	8
laparoscopy	13
appendicectomy	14
kidney operations	2
other	26

Table 5.49 Operative procedures

The grounds given for operation are displayed in Table 5.50 and show that failed medical treatment, uncertain diagnosis, obstruction and peritonitis are the most common reasons for operation. The table is divided into columns and displays the 'reason' compared with 'all operations', the 'first operation' and the 'second and subsequent' operation.

	All Ops		1st Op		2nd & other op	
obstruction	81	18%	43	18%	38	18%
stricture	39	9%	16	7%	23	11%
fistula	53	12%	14	6%	39	18%
abdo mass	46	10%	34	14%	12	6%
abscess	69	15%	22	9%	47	22%
perforation	22	5%	12	5%	10	5%
peritonitis	78	17%	50	21%	28	13%
failed Medic Rx	100	22%	53	22%	47	22%
uncertain diag	122	26%	102	42%	20	9%
growth retard	4	--	3	--	1	--
other	40	9%	23	9%	17	9%
recurrence	--	--	--	--	48	23%
TOTAL OPERATIONS	455		243		212	

Table 5.50 Reason for operation

The table shows that uncertain diagnosis is by far the most commonly stated reason for initial operation. Approximately 20% were found to have failed medical treatment, peritonitis and/or obstruction as a major reason for initial operative intervention. Abscess formation, failed medical treatment and, as one might expect, recurrent disease are the most frequently reported indications for further surgery.

A summary of the different components of these operations is displayed in Table 5.51. The Table reveals that large bowel was resected as often as small bowel while the majority of those undergoing resection had an end to end anastomosis. Very few had an end to side anastomosis - side to side anastomosis being relatively more common.

Although multiple resections are well described only a small percentage in this study had multiple resection, however it was noted that within a single resected segment there were often several discrete areas of disease. Radical resections were performed slightly more often than localised resections demonstrating that surgeons were divided as to which was more successful. The presence of intra-abdominal abscess was

another fairly common finding 12% of operations requiring drainage of some intra-abdominal abscess.

small bowel resection	215	47%
large bowel resection	199	44%
end to end anastomosis	192	42%
end to side anastomosis	8	<10%
side to side anastomosis	21	<10%
one area resected	167	37%
2 areas resected	12	<10%
3 areas resected	4	<10%
local resection	82	18%
radical resection	88	19%
drain abscess	57	12%
ileo/colostomy	76	17%
bypass	18	<10%
laparotomy & biopsy	38	<10%
other	37	<10%

Table 5.51 Operation included

Colostomy or ileostomy was performed on 76 occasions however several of these were re-fashioning of existing stomas. A total of 60 individuals (19%) had a colostomy or ileostomy fashioned at some stage in their disease.

Eight out of the 243 patients having a Crohn's related operation died following the operation (3.3%). However the operative mortality for all the Crohn's related operations was less at 1.7% (8/455). In this group of eight 5 were under 60 and 3 over 60 at the time of diagnosis. It is perhaps also of some note that of the 34 deaths in the Crohn's population 12 were considered directly attributable to Crohn's disease and 8 of these were related to recent operation.

5.9.2 Who Requires Operation

The Crohn's population was divided into two groups those having had an operation and those who had not. The age, sex, site of disease and time to diagnosis were compared in each group to see if these factors influenced whether a patient was likely to require an operation or not (Table 5.52).

	No operation		Operation	
Sex				
Male	29	39%	99	41%
Female	45	61%	143	59%
Age at diagnosis				
<20	19	26%	33	14%
20-39	36	49%	125	52%
40-59	10	14%	55	23%
≥60	8	11%	27	11%
Site of disease				
small bowel	22	30%	75	31%
ileocolic	10	14%	84	35%
large bowel	28	38%	43	18%
discontinuous	13	18%	31	13%
Time to diagnosis				
<6months	42	57%	132	54%
6-11months	9	12%	33	14%
≥12months	18	24%	62	26%

Table 5.52 Associations between operation & no operation

The Table showed that neither the sex nor the time to diagnosis affected the requirement or otherwise of an operation. Figures also demonstrated that fewer of those under 20 at diagnosis required an operation while conversely a higher percentage of the 40-59 group required operative treatment - the difference between the under 20 group and the rest of the Crohn's population was significant ($p < .05$). Finally there was a significant difference between the groups in relation to the site of disease, where it was found that fewer than expected with large bowel disease required an operation ($p < .001$)

when compared against those with disease outwith the large bowel, while many more of those with ileocolic disease, as opposed to other sites, required an operation ($p < .001$). These results suggest operation is most likely in those with ileocolic disease and least likely in large bowel disease. A diagnosis before the age of 20 also reduces the likelihood of an operation.

5.9.3 Operative morbidity

The average number of operations per individual was chosen as a crude measure of patient morbidity. Using this crude indicator it was hoped to identify features known at an early stage which might point to multiple operations and therefore increased morbidity. Factors examined included:

a) time to diagnosis

b) time to 1st operation from diagnosis

c) time to 1st operation from symptom onset

d) sex

e) age at diagnosis

f) site of disease.

Figures displayed in Table 5.53 suggest that the time to diagnosis did not alter the likelihood of the patient requiring at least one operation, between 76% and 79% of individuals having at least one operation in each of the intervals examined. Of those having an operation however a decreasing percentage required a second operation as the time to diagnosis lengthened. The group taking less than 6 months to diagnosis required more operations than those taking greater than 6 months to diagnosis though the differences were not significant. A similar trend is shown when the chance of an individual having 2 operations is examined - this again demonstrates that the shorter the time to diagnosis the more chance there is of having 2 or more operations.

	number of operations				% with		overall
	0		1		2 Ops	3 Ops	chance 2 Ops
Time to diagnosis							
<=6mths (174)	42	24%	132	76%	57	49	43%
7-12mths (42)	9	21%	33	79%	48	50	38%
>12mths (80)	18	28%	62	78%	43	52	33%
Age at diagnosis							
<20 (52)	19	37%	33	63%	61	49	35%
20-39 (161)	36	22%	125	78%	58	46	45%
40-59 (65)	10	15%	55	85%	55	57	46%
>=60 (35)	8	23%	27	77%	22	67	38%
Site of Disease							
small bowel (97)	22	23%	75	77%	55	37	42%
ileocolic (94)	10	11%	84	89%	51	49	44%
Large bowel (71)	28	39%	43	61%	43	47	27%
Discontinuous (44)	13	30%	31	70%	77	67	55%
Sex							
Female (188)	45	24%	143	76%	51	44	39%
Male (128)	29	25%	99	77%	57	55	44%

Table 5.53 Number of Operations

Although the sex of an individual did not affect the probability of a patient requiring an operation a slightly higher proportion of males required 2 or more operations (57% against 51%) - the figures however were not statistically significant.

As previously noted the likelihood of surgery seemed to be related to the age at diagnosis with 85% of the 40-59 group requiring at least one operation compared with 63% of those in the under 20 group. Interestingly, although fewer of those in the under 20 group required an operation more required a subsequent operation when compared with the other groups (61% in <20 group against 45% >20 group). This increase was not related to the number of 'patient years with disease' within each group. Furthermore significantly fewer of the 60 and over age group required a second operation, only one in five, compared with those in the under 60 group ($p < .001$).

The site of disease also had some bearing on the rate of operation. Almost 90% of those with ileocolic disease required operation against 61% of those with large bowel disease. Those with discontinuous disease who had one operation required significantly more second operations (77%) than those with other sites of disease ($p < .001$). Conversely those with large bowel disease required fewer second operations (43%) although this difference was not significant when compared with other sites of disease. Finally, it was noted that if at the time of diagnosis the patient was recognised to have large bowel disease the chance of having two operations was significantly less than those with ileocolic, small bowel and discontinuous disease ($p < .01$).

These figures suggest that if the number of operations is used as a measure of the morbidity of disease then it is better to have large bowel disease be over 60 at diagnosis, be female and have symptoms for a year before diagnosis. Similarly the patient with the greatest 'morbidity' is someone with ileocolic or discontinuous disease who is 40-59 at diagnosis, is male and who has been diagnosed within 6 months of symptom onset.

The pattern of those requiring 2 or more operations is perhaps also worthy of note. Over the period of study of those who required repeat operation 61 had their second and subsequent operations within three years of their first while in 42 at least three years elapsed between first and subsequent operations. Furthermore, only 19 had a second operation within three years and yet later had a subsequent operation at least three years after the first. The longest duration between Crohn's related operations in any patient was 22 years.

5.9.4 Medical Treatment

A simple audit has been kept of commonly used medication. No effort has been made to collect the dose or duration of each different treatment regime nor its efficacy. It is hoped that the prospective phase of the Register might provide more useful information on the efficacy of different treatment regimens over a period of time. The

retrospective audit was therefore carried out to investigate the scope and variability of medical treatment. Despite a careful search of each patient's case record the accuracy and completeness of this audit must be held in some doubt principally because some patients had very few hospital attendances. However, the relative percentages requiring each type of treatment gave some impression as to the extent of drug utilisation in the disease.

	Number n=319	%
none	40	13
anti-diarrheoal	77	24
laxative	15	5
salazopyrin	169	53
steroids	192	60
azothiaprine	56	18
TPN	15	5
vitamins	105	33
antibiotics	37	12
flagyl	24	8

Table 5.54 Frequency of drug utilisation

Table 5.54 shows that 60% of those on the Register had been treated with steroids at one time or another while over half have had salazopyrin. Surprisingly few were noted to require anti-diarrhoeal treatment (24%) and perhaps more interestingly 5% required laxatives. No evidence of specific drug treatment could be found in 13% of those on the Register. Antibiotics were used in a small number of individuals and were more common in those with discontinuous disease rather than small, ileocolic or large bowel disease.

The different types of medical treatment have been compared with the sex, site of disease, age at and time to diagnosis.

It was found that fewer of the elderly group (8/35) required medical therapy when compared with the younger group (32/284). However, the difference barely reaches statistical significance ($p = .05$). Furthermore of those in the elderly group significantly less were treated with salazopyrin and fewer were prescribed steroids or anti-diarrhoeals (Table 5.55).

	≥60		<60		
steroids	16	45%	176	62%	
salazopyrin	12	34%	157	55%	p<.05
anti-diarrhoeal	5	14%	72	25%	

Table 5.55 Medication & Age at Diagnosis

Medication was most frequently used in those with discontinuous disease a greater number in this group requiring anti-diarrhoeals, steroids and/or salazopyrin than in those with a different site of disease (Table 5.56).

	Small bowel		Ileocolic		Large bowel		Discontinuous	
no Rx	19	20%	12	13%	6	9%	2	5%
anti-diarrhoeal	19	29%	24	26%	17	24%	15	34%
steroids	52	53%	59	63%	44	62%	34	77%
salazopyrin	47	48%	48	51%	43	60%	29	65%

Table 5.56 Medication and Site of Disease

Sex and time to diagnosis did not influence the type of medical treatment required by those on the Register.

Summary

Almost 77% of those registered required an operation for their Crohn's disease, 40% had two and 20% three operations described at the time of the survey. The

commonest performed operation was a right hemicolectomy with the most frequent reason for initial operation being uncertain diagnosis. Subsequent surgery was most frequently required for recurrent disease, abscess formation and failed medical therapy.

Operative treatment and 'morbidity' was greatest in males aged 40-59 who were diagnosed less than 6 months after symptom onset with discontinuous disease. Morbidity was least in those females with symptoms for over a year who were diagnosed at 60 years of age or over and who were found to have large bowel disease.

Steroids and salazopyrin have been used in over half of those on the Register. Fewer of the elderly required medication while more of those with discontinuous disease required some form of medical therapy.

CHAPTER 6

DISCUSSION

The work which has been presented has revealed a significant amount of information relating to the diagnosis, further investigation and treatment of Crohn's disease in the population of Tayside. Aspects of this are discussed in this chapter.

The wider implications resulting from the development of the microcomputer system used to facilitate this work are also presented.

6.1. MEDICAL ASPECTS

The introduction has demonstrated how little progress has been made in furthering the understanding of Crohn's disease.

A large number of individuals have looked at specific aspects of the disease for instance evidence of transmissible agents (Heatley 1975), the presence of granuloma in rectal biopsy (Thompson 1981), measurement of disease activity (Harvey 1980) or malignant disease in Crohn's patients (Gyde 1980). However, it appears that although several have described their personal or hospital experience of the disease (Farmer 1981) few groups have produced accurate data using a well defined population (Evans 1964, Maybury 1979, Hellers 1979) - essential if valid and accurate epidemiological information is to be obtained. The lack of progress in our understanding of the disease, despite highly specialised scientific investigation, suggested that a further re-examination of epidemiological data might be worthwhile especially if the powerful data-processing potential of a computer was utilised to investigate the collected data. An accurate epidemiological study would further corroborate the few existing epidemiological reports and provide a valuable contrast to the neighbouring Grampian Region where epidemiological data has been collected for a number of years in a prospective fashion. More particularly however, if this was combined with a comprehensive data collection mechanism based on a computer system containing multifactorial enquiry and analysis

facilities, then previously unrecognised associations may be uncovered which would then merit more careful and intensive investigation.

In order to monitor the disease over a period of years in a prospective fashion it was decided to create an on-going data collection mechanism. Despite the many recognised and previously described problems, a register appeared to be the most valid method for instituting this type of data collection mechanism. The concept of a Crohn's disease Register was therefore born.

The work involved in maintaining such a register would normally be considerable particularly if a large volume of information was to be collected on each patient over a period of years. To help administer this data collection it was decided to investigate the possibility of developing a Register based on a microcomputer system. This would facilitate rapid data processing and subsequent data analysis.

In order to test this working hypothesis a pilot study has been set up to investigate the potential return of such a system. The initial development and retrospective data collection has been used to explore the feasibility and value of the system in terms of its audit and research capability. The system has however been designed to permit the initial retrospective system to be run prospectively. It is hoped that an ever changing dynamic database will be created which will not only continue to provide an audit and research capability but may also help in the management of individual patients.

The initial phase of system development, retrospective data collection, audit and analysis has been completed and the wider implication and application of the system assessed.

6.2 THE REGISTER'S DEVELOPMENT

6.2.1 Case Ascertainment

The early problems with development of the Register related to the definition of what was to be considered a case of Crohn's disease, the retrospective identification of the Crohn's population within Tayside and evolution of the Crohn's data set.

Inaccuracies in the Scottish in-patient morbidity returns have previously been recognised by Lockwood (1971) and more significantly by Patel (1976). Similar substantial inaccuracies in Crohn's disease returns have also been demonstrated (Humphreys 1975, Smith 1975), however, it was felt that this would be the only practical and effective method of initial case capture. In order to use Scottish Morbidity Returns (SMR1) it was therefore felt necessary to firstly validate their accuracy in Tayside. The number of individuals discharged from Tayside hospitals with diagnostic ICD coding of either Crohn's disease, Ulcerative Colitis or Non-Specific Colitis is large. A small pilot study was therefore carried out to investigate the accuracy of each of the three in-patient ICD diagnostic codes within Dundee District. This small study showed that there were a large number of false positives within the group labelled with the Crohn's ICD coding but few false negatives. More significantly all those recognised as false positives at the original admission were eventually labelled with a Crohn's coding during a subsequent admission.

The inaccuracies in SMR1 ICD coding highlight the potential hazards of using these routine statistics as a measure of Crohn's disease within Tayside. These errors further support the inaccuracies in inpatient morbidity statistics reported by other groups such as that of Smith (1975) and Patel (1976). Furthermore if similar discrepancies were present in all SMR1 returns then their value as a basis for future health care planning and distribution of resources must be questioned. These findings also raise the question of responsibility for completion of SMR1 forms. Until recently the method of SMR1

completion in Tayside varied between specialties and departments - a fact which could have led to significant differences in the quality of SMR1 returns.

In order to minimise the proven inaccuracy in Crohn's disease statistics all those given an SMR1 diagnosis of Crohn's disease were subjected to the Register's diagnostic scoring system before being accepted onto the Crohn's disease Register. It is not suggested that this method is infallible, however statistics show that it will be correct in between 93% and 94% of cases. These in-patient statistics have been further checked and supplemented by mailing a list of Crohn's patients to each practice in Tayside requesting confirmation of these cases and the addition of others whom they consider to have the disease. This had the effect of capturing a small number of cases who had not been admitted to hospital, some who have had symptoms for some time but only recently diagnosed and others who have only developed symptoms since 1983 and who are therefore excluded from this present survey. The response to the mailing was excellent with only one practice unhappy to confirm our original list because of the Data Protection Act. Perhaps this good response was due to the fact that good quality data was used in the GP mailing or that Crohn's disease remains one of the few disease's about which so little is known.

6.2.2 Obtaining a working diagnosis for the Crohn's Register

The diagnosis of Crohn's disease is often difficult. A large proportion of those with the disease do however present with a classical history of abdominal pain, weight loss and diarrhoea and the diagnosis is then confirmed by a combination of radiographic, pathological, endoscopic or operative means. There also exists a group in which the symptoms suggest the diagnosis but confirmation is either not conclusive using existing investigative techniques or investigation is frankly misleading. This group, reported as between 10-20% of cases by Morson (1971), lie in a 'grey area' either between inflammatory bowel disease or some other unrelated bowel disorder or between Crohn's disease and Ulcerative Colitis. It is for this reason that scoring systems have been

introduced. Many definitions exist as to what constitutes Crohn's disease (Gjone 1966, Kirsner 1973, Korelitz 1974). Most definitions are simple to implement and relate to the presence of specific radiological, endoscopic or histological findings. The OMGE group have taken a more logical if slightly more complicated approach by calculating the probability of a particular feature being present in Crohn's disease and Ulcerative Colitis (Myren 1979) - a positive score for a finding suggests Crohn's disease while a negative suggests Ulcerative Colitis. A total is calculated for the observed findings, the higher the positive score the greater the probability that the individual has Crohn's while a negative total score suggests Ulcerative Colitis. This method has introduced the concept of weighting to the scoring system. With a calculated accuracy of 93% this appears a realistic and statistically sound approach to diagnosis particularly in the difficult case. Although this system has a predictive value of 93% it has not been designed to separate those individuals who have IBD from those who have a Non-Specific Colitis. This study has shown this distinction to be of some importance as some individuals with ischaemic colitis, radiation proctitis and even endometriosis can have symptoms suggestive of IBD and therefore may inadvertently be submitted to the OMGE scoring system. The author's additional step attempts to predict the liklihood of an individual having IBD and is based on clinical, pathological, radiographic and endoscopic findings. The excellent predictive values using this test, albeit on a relatively small population of patients, were 98% for Crohn's patients and 100% for those with Ulcerative Colitis. The specificity for those with Non-Specific Colitis was 100%. It is to be hoped that others will begin to use this type of scoring system which is indeed only a numerical refinement of other diagnostic criteria (Kyle 1971, Lennard-Jones 1976, Lee 1981) already in use.

The use of the scoring system in this present study has confirmed the OMGE figures. The introduction of the additional step to determine whether or not an individual has inflammatory bowel disease is however considered to be of importance on several counts. Firstly the OMGE group do not appear to have considered this very relevant

point which in this study has resulted in the exclusion of several patients with symptoms highly suggestive of Crohn's disease. Secondly the introduction of this serial type of testing in the scoring system tends to maximise the specificity and predictive value of the performed tests (Fletcher 1984). Experience to date therefore suggests that this system is marginally a more accurate predictor than the original OMGE system.

6.2.3 The Crohn's Database

The development of an appropriate database around which to base the Register was without doubt the most contentious part of the Register's implementation. The collection of diagnostic and basic epidemiological data was considered mandatory and a relevant data set was established without difficulty. However, the greatest dilemma concerned the decision as to what else to collect. Several points required consideration.

Firstly the idea of the Register was to produce a general overview of the disease for Tayside. This would necessitate the collection of a large data set covering many aspects of the disease - the collection of such a broad based data set as far as the author is aware has not previously been attempted. It was this concept that would then permit a wide ranging enquiry from which any apparent associations revealed could be further investigated from within the Register's database.

Secondly although the Register was to be implemented using a retrospective data collection mechanism it was hoped to continue the data collection prospectively. A continuous on-going data collection system would therefore evolve enabling the Register to provide information on the disease over a period of years. It was therefore important to structure the data in a way that would lend itself to easy collection and entry into the computer's database.

Finally, it was equally important not to fall into the trap of collecting everything that was thought 'might be of value'. To attempt this would result in an unmanageable database.

Overall the chosen format, with separate distinct groups of data for recurring and non-recurring information, has certainly stood up to the initial retrospective data capture. The retrospective proforma questionnaires (appendix 5)have been shown to be more than adequate and should with a few minor alterations be satisfactory for use in prospective data collection. Much thought has also gone into the prospective contact form which will utilise elements of appendix 1a,b,c,2,3,4 & 6b. It is hoped to use parts of appendix 3,4,6a,b,c for follow up data to be used both in clinics or as a periodic mailing.

The analysis of the retrospective database has demonstrated the value of the initial data set. The major proportion of this data has been shown to be of proven value and will continue to be collected in the prospective phase. Minor and irritating difficulties with the data set included the failure to use the occupational groups generated by the Registrar General and the difficulty in assessing social class from information supplied in case records. With the benefit of hindsight it is now felt that more time should have been spent in assessing available health-care related and census statistics produced for each geographical area. More of the health statistics produced for Tayside could then have been used, for instance occupation and type of dwelling, as the control group enabling direct comparison with the Crohn's population.

Major changes will be made in the 'Investigation' part of the data set where some biochemical information will be dropped including urea and electrolytes - though retaining liver function tests. Similarly it is hoped to monitor serum iron, B_{12} and folate as recurring data as opposed to initial diagnostic data.

Furthermore the retrospective collection of endoscopy data has shown that endoscopy reporting is sadly lacking in accuracy and consistency - probably a result of the large numbers of clinicians performing the investigations. Much more valuable data could

be obtained from the endoscopies in respect of audit and research if a more structured report format was introduced. This highlights several problems when attempting clinical audit within the health service. Firstly the accuracy and consistency of initial data recording must be considered. The transcription and interpretation of this recording must then be closely monitored to ensure that clinical findings for instance diagnostic category fit into one of the recognisable standard diagnostic groups. Indeed the author is presently involved in introducing a new system for recording all endoscopy data produced in the clinical measurement area in Ninewells hospital. This includes the implementation of a computer system based on the facilities contained in the Register. Aspects of this development will be discussed later in this chapter.

The data set used for both pathological and radiological investigation will be retained without change. Analysis of these aspects have been fruitful. One interesting observation in this section was the finding that the diagnostic index from the Pathology department did not always correlate with the Register's diagnosis. This is perhaps to be expected as there are often no specific indicators of disease and lends support to the idea and value of serial diagnostic testing in this disease. Reporting of radiological investigations was on the whole more consistent. More valuable information could therefore be extracted from the database. The time involved in collecting this data would have been greatly reduced if there had been a computerised index within the radiology department. This type of index would be invaluable in monitoring the cost effectiveness of the many expensive investigations performed, particularly in the present economic climate, as well as providing important data on which to base and help in clinical research. Indeed our initial survey of the investigations performed on the Crohn's patients suggests an ever decreasing positive return over recent years for barium studies. This need not however, necessarily imply a waste of resources as a negative x-ray may represent a very positive result in a patient's management.

Few changes would be made to the treatment side of the database in any prospective phase. The operative data set was found to be concise and provided a chronological sequence of operative events for each registered individual. By contrast little valuable data has emerged from the retrospective collection of medical treatment data; however as the quality of collected data relating to medical treatment improved during the prospective phase it will be possible to explore the use and efficacy of treatment regimes using disease activity and morbidity scores.

Specific extra data items which will be included in prospective collection include the number of hospital admissions, days in hospital, consultant responsible for patient and date last seen by a hospital doctor. The weight of the patient will also be recorded as a recurring piece of data. Provision will be made within the database for a regular comments section and a number of 'blank markers' will also be included.

These markers could at any stage be given a specific meaning (eg. entered into drug trial or on sugar free diet) without altering the database structure.

The inclusion of this extensive and yet expandable data set in conjunction with the available computing facilities has created the equivalent of a Crohn's disease patient management system based on a microcomputer. Patients can be registered with the system, then followed over the years, data being added to their file structure every time they visit outpatients or following hospital admission. Data on the system can then be used to prompt events or some action for instance a clinic visit or reminders to patient, general practitioner or hospital doctor that a patient has not been reviewed for perhaps three years. All the data generated in the patient management phase is then available for routine or ad-hoc audit and indeed can be used as the basis of further research if appropriate.

In summary, although many groups have collected data on diverse aspects of Crohn's disease none, as far as the author can ascertain, have accumulated and collated

such an extensive and wide ranging data set. It is suggested that this offers a significant overview of the disease, the findings of which are now discussed.

6.3 FINDINGS OF THE RETROSPECTIVE ANALYSIS OF THE REGISTER

6.3.1 Epidemiological findings

In order to obtain valid epidemiological information using a retrospective case study it is important first to define exactly what the study considers to be a case of Crohn's disease and secondly to define the control group (Mausner 1974).

The author has attempted to overcome the first of these problems by adapting the OMGE scoring system as previously described.

Gilat (1983) has suggested that epidemiological data generated from accurate population studies of Crohn's disease could act as a 'gold standard' for the disease. The patient group was collected from the whole of Tayside and the general population used as the control group. Use of the general population as the control group permitted the Crohn's group to be compared with a well defined population, imperative if accurate epidemiological data was to be obtained. This facilitated the use of routine statistics produced for Tayside Region by the Registrar's Office . Tayside is a good area for epidemiological study, firstly because the population of the area has remained static over the past 90 years (394,824 / 388,433 / 397,605 / 391,846 for 1891, 1921, 1971 & 1981 respectively). Secondly, examination of cross boundary flow statistics shows that Tayside health authority is a net importer of 50,000 patients from neighbouring Fife and Grampian region - estimated 1983 population 394,895 actual catchment population 445,249 - it is therefore unlikely that any patient with Crohn's disease resident in Tayside will be seen in hospitals outside the area. Specific figures for cross boundary flow for Crohn's disease reflect the general trends. Furthermore in an effort to ensure complete data collection, information has been obtained from several sources. Of equal importance is the accuracy of diagnosis in each potential Crohn's patient; great care has therefore been taken to ensure this accuracy by examining each candidates case record carefully.

The gradual increase in incidence observed in many studies (Gilat 1979, Maybury 1979, Gilat 1982) has been confirmed by this study. The apparent reduction in

this increase in Tayside during the late 1970's has also been noted elsewhere by others (Hellers 1979, Medeloff 1982). Analysis has shown that variation in the definition of disease onset does have some effect on calculated incidence rates. Figures (Table 5.1) showed that only 75% of individuals developing symptoms within any 4 year period will be diagnosed within that period. A lag period of 4 years must elapse before over 95% of those developing symptoms within the original 4 year period have in fact presented and been diagnosed with the disease.

The Crohn's population of Tayside compares favourably with most other epidemiological studies however it contrasts with the neighbouring Grampian population. Interestingly the calculated incidence figures for Tayside as a whole, for Arbroath and figures obtained from Grampian region all show considerable variation. Why there should be such variation in adjacent geographical areas is a point which requires closer investigation. Comparison of the Tayside and Grampian region show similar trends for both areas with an apparent lead of some 10 years in Grampian (fig 6.1). It will be interesting to observe the Arbroath figures over the next few years to see if they also plateau. This demonstrates the variability of the disease even in neighbouring areas. It is perhaps unwise to speculate whether the recent increased prosperity in the North East may be partly responsible for the apparent ten year difference in trends between Grampian and Tayside.

These findings certainly require further investigation. The first step should be to confirm that the method of case ascertainment and diagnostic criteria are comparable and therefore the differences noted authentic. Initial enquiry suggests that the studies are likely to be comparable. A further more specific epidemiological survey could then be undertaken using groups of Crohn's patients and groups of 'normal' patients from each of the three areas concerned (Tayside (except Arbroath), Grampian and Arbroath)

Trends in incidence

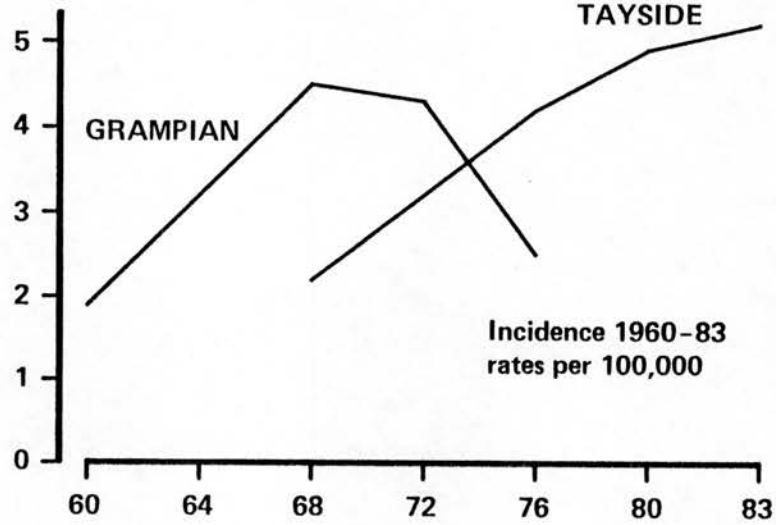


Figure 6.1

Use of the computer system has enabled the point prevalence to be calculated for each 4 year period without difficulty. The prevalence rate per 100,000 has steadily increased over the 16 year period and continues to rise. The rates compare favourably with Aberdeen 32.5 (Kyle 1971), Uppsala 50 (Bergman 1973) and Malmo 75 (Brahme 1973) (all per 100,000). There appears to be no other study available to compare point prevalence calculated at 4 yearly intervals although the group in Malmo measured point prevalence at several stages of their study (Brahme 1973). The increase we have shown is consistent with the chronic nature of the disease and its low mortality even in the elderly patient.

The clustering observed in the Arbroath area merits further investigation. The prevalence of the disease is recognised to be higher in the more densely populated industrialised centres (Kyle 1971, Bergman 1975, Maybury 1979) than in rural areas. However it should be noted that many of these centres, like Arbroath, are situated on the coast where intake of fish and seafood products is likely to be high. Initial enquiry has also revealed that the domestic water supply to the Arbroath postcode area is only partially treated being the only part of the region which does not draw any of its water from the main regional purification plant. Furthermore this supply has a high lead concentration and since the early 70's - as a result of EEC regulations - has required the addition of lime to reduce the acidity and hence the lead concentration. It is perhaps speculative to suggest that lead, which is recognised as a cause of gastrointestinal mucosal damage, may be one of the factors contributing to the increased incidence in this area.

The majority of studies, for example Smith (1975), Miller (1974) and this present study, show an overall preponderance of females however figures presented here have shown that there is a significant shift in the sex ratio towards males within Tayside particularly over the last 4 year period under study. The number of males increased significantly over this period, furthermore this type of change was also noted in Grampian region some 10 years ago. Once again these changes appear most marked in the

Arbroath area where, despite the relatively small numbers involved, there has been a marked increase in the number of males over the past 8 years. The reason for this variation remains unclear for both the Tayside and Arbroath populations are matched for sex with the ratios for male/female being .471, .476 and .475 in Tayside for years 1961, 1971, 1981 respectively while in Arbroath the male/female ratio was .474 in 1971 and .471 in 1981.

The low familial incidence in Tayside is in sharp contrast to Kisner (1973) Chicago and Korelitz (1981) New York but similar to that seen by Kyle (1971) in Aberdeen.

The significant increase in large bowel disease has previously been well described (Kyle 1971, Hellers 1979, Mendeloff 1980, Weterman 1981). This increase appears more prevalent in the elderly Crohn's patient - a feature also described by other groups (Brahme 1975, Maybury 1979, Carr 1982). The Tayside figures also show that there has been a real increase in incidence in large bowel disease in the elderly over the 16 year period and confirms that this is a more significant rise than that found for the rest of the Crohn's population. This elderly group reveals several other interesting features.

Only a few studies have examined the elderly group of Crohn's patients in a defined population. The Birmingham group (Fabricus 1985) found 8% of the overall population to be over the age of 60 at the time of diagnosis, a figure which is similar to that for Tayside and that of Goligher (1980). The Tayside figures also show a definite increase in incidence over the 16 year period under study and confirm that the increase in numbers of aged patients is not fully explained by an aging population. Kyle (1971), Miller (1974) also showed an increasing number of elderly Crohn's patients and similarly found that there was a preponderance of females in this elderly group. Although Carr (1985) noted a similar proportion of elderly women with inflammatory bowel disease the very high proportion of women in this series, even allowing for the increased proportion

of women expected in this elderly group, has not previously been reported and requires confirmation by other groups.

There appear to be no comparable figures for mode of initial presentation although the relatively high emergency presentation is perhaps surprising. Despite a greater awareness and an increasing availability of investigations the time taken from onset of symptoms to diagnosis has not changed over the 16 year period suggesting that neither an increasing awareness nor the advent of endoscopy has significantly affected the recognised increase in incidence.

The epidemiological review therefore suggests that the incidence rates in neighbouring areas, the elderly Crohn's population and the group resident in the Arbroath area merit closer investigation and examination.

6.3.2 Investigations

Pathology

The pathology audit identified almost 700 Crohn's related specimens from these patients of which 350 demonstrated features indicative of Crohn's disease. Further analysis appears to reflect the changing trend in incidence with an apparent slowing in the increase of both samples submitted and number of positive reports over the past 4 years. The relative increase in the proportion of biopsy specimens submitted is also noted and probably reflects the increasing role of endoscopic investigation in the Crohn's patient.

The distribution by site and macroscopic findings of submitted specimens in this study are similar to those found by other groups (Farmer 1975). The majority of resected specimens contained either segments of ileum and/or right colon while the common macroscopic findings included thickening of the bowel wall, narrowing, lymphadenopathy, mucosal ulceration and serosal injection. Transmural inflammation, granuloma formation and the presence of giant cells remain the most useful microscopic

pointers to the disease. Overall, the frequency of these histological findings were similar to those of other groups (Cook 1973, Chambers 1979, Mekhjian 1979). Although evidence of granuloma formation was found in only 34% of specimens examined 56% of those on the Register demonstrated granuloma formation at some point in their disease. Similar figures were noted by Piris (1983), who reported 50%, and Thompson (1983), who described some 62%, with granuloma formation.

Examination of the submitted specimens by patient revealed that 90% of those registered have had at least one specimen submitted for histological examination - of this group 80% demonstrated positive evidence of Crohn's disease. For slightly less than one quarter of those with histological evidence of disease the diagnosis was based on biopsy only, whereas the diagnosis for the remainder was based on both macro and microscopic examination.

It has been shown that a histological diagnosis is more common in those diagnosed under 20yrs or 60yrs of age and over. The increased frequency of histological diagnosis in the elderly group is probably explained by the relatively large number with large bowel disease and subsequent ease of endoscopic biopsy.

The presence of rectal bleeding is a strong indicator that histological evidence of disease will be obtained. It should also be remembered that 59% of this group had large bowel disease. Furthermore histological evidence of disease was more common in those with symptoms for 6-11 months before diagnosis.

More significantly perhaps was the finding of inflammatory changes and granuloma in the rectum and anal canal in a sizeable percentage of those patients considered to have ileocolic and small bowel disease. Of similar note were the 20% of individuals with discontinuous disease who had chronic inflammatory changes in the duodenum.

Granuloma are recognised to be present in the early part of the disease (Warren 1948, Chambers 1978). The Tayside figures suggest that the optimum time for

identifying granuloma formation is between 6 and 11 months after symptom onset. Further interesting findings were demonstrated when this group was examined in more detail. Although there was no difference in the proportion of males and females with granuloma formation it was clear that there were differences between the male and female groups. Significantly more females with granulomas had large bowel disease and a greater proportion were aged 60 or over at diagnosis.

Evidence of granuloma formation is recognised as a good indicator of Crohn's disease (Morson 1972 Cooke 1973, Farmer 1968) however it is clear from this study that even in patients with Crohn's disease slightly less than 50% of gross specimens showed evidence of granuloma formation on microscopy. Although Chambers and Morson (1980) emphasise the value of large bowel biopsy they found, as in this study, that no more than 20% of specimens demonstrated evidence of granuloma - this it must be remembered is in patients with known Crohn's disease. It has also been suggested that granuloma formation is a good prognostic indicator (Glass 1976, Chambers 1979) however the Tayside figures suggest that those with granuloma have a greater morbidity both in terms of hospital admissions and re-operation.

Radiology

Despite recent advances in the radiological techniques used in the investigation of Crohn's disease which include such techniques as ultrasound (Bluth 1979), indium scans (Saverymuttu 1983) and computer tomography (Goldberg 1983) the mainstays of radiological investigation remain the barium meal & follow through, the small bowel enema, which is being increasingly used, and the standard barium enema.

The radiological findings in Crohn's disease are known to fluctuate widely (Brahme 1975, Marshak 1976). This study demonstrates some of these features and reports on a variety of findings related to the radiological investigation of Crohn's disease in Tayside.

Perhaps of most interest in the radiological audit were the figures confirming the large number of barium studies performed and reported as showing no abnormality in those known to have Crohn's disease. Just less than one third of all barium studies were reported as normal - figures which confirm the fluctuating nature of some of the radiological changes associated with the disease. More significant than the number of normal barium studies performed in this group however, were the ratios associated with the changing trends of normal/abnormal and normal/Crohn's investigations over the period of study. The change was most pronounced in the normal/Crohn's features where the ratio of normal to Crohn's increased as shown in Table 6.1

	Crohn's features	Normal appearance	ratios
64-67	6	1	6:1
72-75	3	2	3:2
80-83	2	3	2:3

Table 6.1 Ratios normal/Crohn's features

As one would expect there were only a few patients on the Register with no evidence of a Crohn's related radiological investigation. Almost 80% of those Crohn's patients undergoing radiological investigation were found to have some radiological evidence of inflammatory bowel disease. The great majority (90%) not only had findings supportive of Crohn's disease but also demonstrated these findings at the time of diagnosis. The smallish number who were subsequently shown to have evidence of disease on x-ray confirm the fluctuating and often rapidly changing nature of the radiological features of the disease (Jones 1969, Brahme 1970).

Of the 47% of all barium studies which were reported as showing evidence of Crohn's disease the majority (61%) were obtained from barium meal & follow through examinations, 29% from barium enema procedures and only 9% from small bowel enemas. The surprisingly small percentage of small bowel enemas is probably a reflection

of the numbers of these investigations performed. Furthermore and unexpectedly the relative diagnostic return for the small bowel enema is less than that of barium meal and follow-through. This is surprising because the former is commonly accepted to be more accurate by many clinicians (Truelove 1981, Keddie 1982). The reason for the poorer diagnostic return in this area could well be explained by the fact that this investigation is kept mainly for the difficult case where other barium studies have shown no evidence of disease.

Although only 29% of positive barium investigations were from barium enema examination the number of individuals eventually showing evidence of Crohn's disease on barium enema was higher at 42%. Of some diagnostic value was the finding that in the elderly Crohn's patient barium enema gave the best diagnostic return even though fewer had positive radiological investigations (12/35). Of further note was the finding that 20% of those with evidence of disease on barium enema had evidence of disease in the small bowel, and a similar percentage had small bowel studies demonstrating disease in the large bowel.

The nature and reported frequency of specific features found on barium investigation is similar to that reported by others (Marshak 1955, Nolan 1980). The relative rarity in the reporting of certain radiological features in this study is also of interest. Of note were the few with 'skip areas' - reported elsewhere as 10% (Kyle 1972) - 'fistula formation' - also uncommon - and the 'cobblestone appearance'; all are normally recognised to be more common (Nolan 1980) than in this study. This inconsistency might well be due to observer error and might disappear if each of the radiological investigations were reviewed by a radiologist with a specific interest in Inflammatory Bowel Disease

Closer examination of the group with radiological evidence of disease revealed several other interesting findings. Figures showed that the 20-39 age group most

commonly had a radiological diagnosis (75%) while the over 60 age group were shown to have a radiological diagnosis in less than a third of cases. In addition it was clear that those with large bowel disease only demonstrated radiological evidence of disease in 25% of cases which is in marked contrast to the 80-90% figure suggested by Kyle (1972).

Goldberg (1981) has previously noted the value of retrograde filling of the terminal ileum by barium enema a finding which perhaps reflects damage to the ileocaecal valve from a diseased distal ileum.

Endoscopy

Since the introduction of the fibreoptic endoscope in 1958 (Hirschowitz 1958) its use in gastroenterology has expanded rapidly. The first colonoscopes were introduced in Europe in the early 1970's and as the instruments have improved so the number of investigations has increased. Although the colonoscope allows examination of the whole colon - and even the terminal ileum (Gabriellson 1977) - it is not an essential component of the investigation of the Crohn's patient (Williams 1978) even though it can be performed with relative ease in most patients (Geboes 1975).

While the Tayside endoscopy audit was incomplete it was adequate to demonstrate the increasing trends in endoscopic procedures over the period under study.

The endoscopic findings in both colonoscopy and sigmoidoscopy were on the whole very non-specific with the classical 'cobblestone' appearance, recognised to be an important diagnostic finding (Williams 1978, Waye 1980) being very rare. The presence of the apthoid ulcer - acknowledged to be an early endoscopic feature of the disease (Morson 1972) - was similarly uncommon or at least recognised only rarely.

Although 60% of individuals were noted to have some inflammatory changes at sigmoidoscopy or colonoscopy fewer than 20% of endoscopies performed in the Crohn's patients merited an endoscopic diagnosis of Crohn's disease. Similar non-specific changes on rectal biopsy have been noted in those with small bowel disease (Dyer 1970) while Kyle (1972) described as many as 75% of those with large bowel disease with

non-specific changes on endoscopic biopsy. The small number whose findings merited a diagnosis of Crohn's disease supports the views of Axon & Dickson (1983) who suggest it unwise to make a Crohn's diagnosis based purely on endoscopic features alone. Further support for this view is demonstrated by the fact that only 47% and 33% of those with confirmed pathological and radiological changes of disease were shown to have endoscopic changes in the large bowel.

Findings however emphasise the importance of biopsy and confirm that changes are relatively common in the anal canal, rectum and colon in cases of small bowel disease. Although evidence of inflammatory changes on endoscopy in the Tayside Crohn's population was similar to that found by Hogan & Hensley (1980) the Tayside figures suggest that inflammatory changes on sigmoidoscopy in the elderly group were more common than in the younger patients. These findings were similar to those of Hill (1979) who suggested that this was a simple reflection of the frequency of large bowel disease in this group.

It was perhaps not surprising that 90% of those with rectal bleeding showed large bowel endoscopic changes. This figure was contrasted by the few with diarrhoea that showed similar changes.

Slightly less than half of the Crohn's patients who had a gastroscopy had evidence of inflammatory changes - as one might expect 35% of this group had discontinuous disease. Fielding (1971) suggested that there was some evidence that peptic ulcer disease was more common in Crohn's patients however the lack of histology in many of those undergoing gastroscopy makes any clear statement on this finding unwise. The non-specific findings however tended to confirm the view that gastro-duodenal changes although not particularly common are easily recognised (Danzi 1976).

Haematology/Biochemistry

Although alterations will be made to this data set as the register is continued prospectively the retrospective analysis of data revealed some interesting features. The

majority of abnormal results at diagnosis related to ESR and white blood cell count (WBC) which were both raised. Kyle (1972) in his series noted that 85% of individuals had an ESR of 20mm/hr or more - similar to Krause (1971) in Uppsala. The WBC values also compare favourably with Kyle's series when the number of individuals with WBC counts of 12,000/mm^3 or more were compared. Haemoglobin (Hb) results were commonly in the normal range, with a mean of 12.25gm/dl, not only at diagnosis but through the whole period of disease. This was in marked contrast to Kyle (1972), who found a mean Hb value of 10.4gm/dl, Fielding (1971), who found two thirds of his series with a Hb value of less than 12.5gm/dl when the disease was active and Beekin (1975) who noted over half his patients became anaemic. There was no variation in any of the other parameters measured over the period of the disease.

More interesting perhaps were the low serum concentrations of vitamins and iron noted at the time of diagnosis. Low serum folate measurements are well recognised (Hoffbrand 1968, Smith 1971, Elsborg 1979) however it must also be noted that treatment with sulphasalazine may compound the recognised reduced folic acid absorption because of mild drug induced haemolysis. Even in the group diagnosed within 6 months of symptom onset a large number were found with low folate, iron and/or Total Iron Binding Capacity (TIBC) levels (65% folate, 72% iron 43% TIBC) suggesting that functional changes in the mucosa may well exist for some time before symptoms of the disease develop.

As one would expect, there were more in the elderly group with protein levels below the normal range - the result of loss from the gut and normal physiological response to aging. More of the younger group have discontinuous disease and therefore have several non contiguous areas of disease which probably accounts for the relatively high numbers (40%) with low albumin. Surprisingly the time taken to diagnosis did not appear to correlate with the number of individuals with low albumin or protein levels. Low protein/albumin levels in those with small bowel and discontinuous disease have

however been previously described Cooke (1974) and probably relate to the severity of disease.

6.3.3 Treatment

Operative.

The 77% requiring surgery in the Tayside series is similar to that described by Fielding (1972) and Farmer (1975). The high crude re-operative rate in this series is confirmed by Higgens (1980) who using actuarial methods found that similar numbers required a second, and then a third operation. Greenstein (1975) also using these methods found that the numbers requiring further operation rose with each operation. Indeed at the time when the analysis of treatment was performed 20% of those on the register had at least 3 operations. These figures demonstrate the not inconsiderable morbidity caused by operation and re-operation on those with the disease. As one might expect right hemicolectomy was the most common procedure accounting for almost 25% of all operations performed. This figure reflects the numbers who have distal ileal or ileocolic-colic disease and the fact that colonic disease on the whole carries a better prognosis (Allen 1986).

In Tayside a relatively large number of patients required their first operation because of uncertain diagnosis (42%) and/or peritonitis (27%). They probably reflect the not inconsiderable number of patients (30%) who presented acutely and required laparotomy for both diagnostic and therapeutic reasons as an emergency or semi-elective procedure. This to some extent contrasts with the views of others (Fazio 1983 Brooke 1977) who suggest that operation can almost always be performed electively except in the presence of acute complications. Figures also confirm what others have shown (Kyle 1972, Brooke 1977, Farmer 1975) that obstruction, stricture formation, failed medical treatment, abscess formation and fistula formation are the major causes for operative intervention. It is also evident from this data that operation played a major role in the diagnosis of 143 patients.

As one would expect recurrence of disease is the prime reason for second and subsequent operation although failed medical treatment is once again common. Abscess and fistula formation also cause an increasing number of individuals to have further operations.

The few by-pass procedures performed suggest that most surgeons in Tayside accept that resection is superior to by-pass (Alexander-Williams 1972, Homan 1978). Analysis also shows that segments of small and large bowel (very often in combination) are resected in equal numbers. It is also clear that end to end anastomosis is used in over 90% of bowel resections and that although segmental disease is not uncommon, most surgeons, at least in this area, where possible attempt to include all the diseased areas in one segment thus avoiding the need for multiple anastomosis. Brooke (1977) suggested that for small bowel or localised large bowel disease the minimum resection should be carried out with end to end anastomosis. This preserved bowel and avoided blind ends which can predispose to steattorrhoea while for more generalised disease colectomy should be performed. The recent practice of stricturoplasty used by some, including Williams in Birmingham, has not been tried in this area.

Colostomies and / or ileostomies were fashioned relatively frequently, 25% of individuals on the Register had a stoma at some point in their disease, figures which are borne out by others but particularly Farmer (1976).

Closer scrutiny of the data showed that there is no difference in the sex or time to diagnosis of those requiring surgery. It is however noticeable that although fewer of the under 20 group required operation they coincidentally were more likely to have a second procedure, a finding previously noted by de Dombal (1971), than any other of the age groups. Why the 40-59 age group are more likely to require an operation than the other age groups is unclear.

One valuable statistic to emerge as far as long term morbidity is concerned was that significantly fewer patients with large bowel disease required one operation

($p < .001$) and then subsequent operations. Conversely, significantly more of the group with small bowel disease required surgery ($p < .001$) and overall had more operations - facts which have been previously recognised by Farmer (1975) and Hellars (1979). One further measure of potential morbidity relates to the length of time to diagnosis. As this time increases the percentage of the group with one operation who subsequently required a second operation decreased, and secondly, the overall percentage risk of requiring two operations at the point of diagnosis also decreased. It therefore appears that time to diagnosis may also be an indicator of long term morbidity.

The age at diagnosis similarly reflects the chance of 2 operations, for almost 1 in 2 of the 20-39 group required 2 operations against 1 in 5 of the 60 and over age group. Furthermore this study confirms the findings of Fabricus (1985) that elderly patients (60 years and over) are less likely to require surgery than those in the under 60 group, particularly if they have large bowel disease. As in de Dombals series (1971) and the Birmingham series (Fabricus 1985) we found that this elderly group rarely required further surgery for treatment of their disease.

These findings suggest that if the number of operations is used as a measure of morbidity then those with the least morbidity are those that take 6 months or more to be diagnosed, have large bowel disease and are 60 and over at diagnosis. Similarly the patient with the potentially greatest morbidity at the time of diagnosis is the individual who is diagnosed within 6 months of symptom onset, has ileocolic-colic or discontinuous disease, is male and between the age of 40-59 at diagnosis.

Medical management

Review of medical therapies used in Crohn's disease illustrates our lack of understanding of the disease process. A multitude of therapies have been used and although patients have improved on each therapy, controlled trials have often failed to confirm the occasional successful case report. However steroids (Malchow 1984),

azothiaprine / mercaptopurine (Wiloughby 1971), sulphasalazine (Summers 1979), metronidazole (Ursing 1975) and total parenteral nutrition (Elson 1980) are all recognised to help under different circumstances. Levamisole (Wesdorp 1978), cromoglycate (Williams 1980), Vitamin A (Wright 1985) oral BCG vaccine (Burnham 1979) and many others have been tried without proven success other than the occasional anecdotal improvement.

Although no measure of efficacy could be made on the different types of medical treatment used during the period of study several interesting findings emerged from the audit of medical treatment. Over half of those registered required steroids and or salazopyrin, however some 40 patients as far as could be ascertained had not required specific medication for their disease. A surprisingly small number were noted to require anti-diarrhoeal medication while 5% were known to have taken laxatives at some point in their disease.

Sex and time to diagnosis showed no association with the types of medication required to control the disease. However, it was apparent that fewer of the elderly Crohn's population were prescribed or required steroids, salazopyrin and anti-diarrhoeal medication. Similarly, and as one might expect, more of those with discontinuous disease required steroids, salazopyrin and anti-diarrhoeal medication to control their symptoms.

The value of this retrospective audit of medical treatments has therefore been small. The importance of this section however, is in the mechanism that has been created which will, in the prospective phase, permit some measure of the efficacy of specific treatments and enable controlled trials to be undertaken on groups selected from the database.

6.4 FUTURE DEVELOPMENT OF THE REGISTER

The development of the computerised register and the subsequent analysis of the retrospective data clearly demonstrates that this type of computerised disease register can readily be developed and managed on a microcomputer. The system operates successfully with the large storage capacity of the hard discs now commonly used in microcomputers. The speed of operation of the system, perhaps a little slow during complex analysis operations, is more than offset by the flexible nature of the data manipulation and enquiry facilities.

More of a problem however will be the practicalities of setting up a scheme of operation for the prospective development of the Register. Several points have emerged while implementing the Register retrospectively. Firstly it was clear that many of the clinicians in the area looked after what were often small groups of the Crohn's population. Furthermore although there were several recognised gastrointestinal outpatient clinics each had a number of Crohn's patients as regular attenders. There was no specific inflammatory bowel disease clinic which would have made the introduction of the prospective Register a much easier task.

Even with the best intentions it was felt unlikely that all clinicians involved in the care of Crohn's patients would regularly remember to complete proformas or conform to the required protocol which would enable the Register to develop in a prospective fashion. This would create a situation where the Register would become incomplete and therefore inaccurate and by the Registers own defined criteria would merit its closure.

Other methods of implementing the Register have therefore been explored. The most practical of these appears to be a compromise and would involve a Register 'controller', who would be a doctor, paramedic or medical secretary, working perhaps five half days a week in conjunction with several 'enthusiastic' clinicians. Patients would be identified from proformas returned to the Register controller from the wards and clinics

by those participating in the Register scheme. Other patients would be 'captured' as they were filed with the health board morbidity returns. The name and CHI number of each individual with a Crohn's or related ICD code being relayed to the Register controller for further investigation. This would not only allow the identification of those with Crohn's disease but would also facilitate the identification of all those with inflammatory bowel disease thus promoting the development of a truly prospective Register for inflammatory bowel disease. This would have obvious advantages over the present Crohn's disease Register.

Individuals who went for prolonged periods without further addition to their existing data set could periodically be mailed to enquire about their progress. This facility could also be used to undertake periodic but regular checks on disease activity and morbidity of all those remaining 'active' on the Register. An example of the type of proposed 'mailing questionnaire' is shown in appendix 6a & 6b and could be combined with a periodic morbidity questionnaire (appendix 6c). It is felt that with this approach and using pathological and radiological reports as validity checks to the primary data capture process the Register could function in a prospective manner.

Although the database was created with prospective data collection in mind several other data items would require to be added to the data set to enable those with Ulcerative Colitis and Non-Specific Colitis to be identified within the system. It is proposed that those with Ulcerative Colitis would have a data set similar to those with Crohn's disease but the non-specific colitics would have a small subset of the overall data set. Additional information would also be collected concerning the number of times patients were admitted and the number of inpatient days that accrued through these admissions.

6.5 THE VALUE AND IMPLICATIONS OF THE COMPUTER SYSTEM

The initial data input from the retrospective data collection has shown that the computer system is both easy to use and effective and proficient in its operation. The specialised repertoire of data types for the efficient storage of clinical information has well matched the data set required. The flexibility of the 'input form' concept whereby information relating to one type of data transaction, for instance 'take-on' or 'repeat investigation', has been of considerable value. Furthermore the inclusion of several steps which check the validity of data entered into the database - a major concern with any data collection mechanism - has prevented the collection of any 'hash data'.

Analysis of the retrospective data has clearly shown that the data manipulation facilities are powerful tools. The subset facility, which enables individuals to be grouped by certain user defined criteria (ie males with large bowel disease and over 60 at diagnosis), has given extra power to the data processing capability of the system and greatly enhanced its analytical potential. When the numerical and non-numerical audit routines are used in conjunction with the subset routines a rapid, powerful and versatile audit tool emerges. Any data item held on the Register can be analysed by one or combinations of these utilities. The value of this facility is maximised when performing specific types of complex audits. For instance the site of disease and age groups at diagnosis can be displayed in one table (Fig 6.2). Note each age group has been created as an individual subset.

The enquiry and evaluation performed on the Crohn's population using the analytical facilities has also demonstrated the potential value of the Register as a research tool. The initial idea of providing an overview of the disease on which further more specific research might be based has been established. The discovery of the high frequency of Crohn's disease in the Arbroath area and the differences in the elderly Crohn's population are probably the clearest examples of this concept to date.

TABULAR DATA PRESENTATION AND ANALYSIS

Site disease & Age at diagnosis

313 data points from a Sample of 313 subjects
Sample is from a population of 317 selected from 4 subsets

KEY for X axis

Code and subset name
A = <20 at diag(52) 19/1
B = 20 to 39 at diag(161) 20/1
C = 40 to 59 at diag(65) 20/1
D = >=60 at diag(35) 19/1

KEY for Y axis

Field 36 in File crohns:cinv - EXTENT DISEASE
1 = SMALL BOWEL
2 = ILEO COLIC
3 = LARGE BOWEL
4 = DISCONTIN DISEASE

		E	A	B	C	D		TOTAL
	N!	0	1	5	4	1	!	11
E	%R!	0.0	9.1	45.5	36.4	9.1	!	
	%C!	0.0	1.9	3.1	6.2	2.9	!	4%
	N!	0	9	52	23	12	!	96
1	%R!	0.0	9.4	54.2	24.0	12.5	!	
	%C!	0.0	17.3	32.3	35.4	34.3	!	31%
	N!	0	14	62	14	4	!	94
2	%R!	0.0	14.9	66.0	14.9	4.3	!	
	%C!	0.0	26.9	38.5	21.5	11.4	!	30%T
	N!	0	12	21	21	16	!	70
3	%R!	0.0	17.1	30.0	30.0	22.9	!	
	%C!	0.0	23.1	13.0	32.3	45.7	!	22%T
	N!	0	16	21	3	2	!	42
4	%R!	0.0	38.1	50.0	7.1	4.8	!	
	%C!	0.0	30.8	13.0	4.6	5.7	!	13%T
TOTAL!		0	52	161	65	35	!	313
	%T!	0.0	16.6	51.4	20.8	11.2		

N = number
E = empty fields

%T = % of Total
%C = Number as N% of Column total
%R = Number as N% OF Row total

Age groups and Sex

Figure 6.2

The retrospective analysis and data collection has not been concerned with patient management. It is clear however, that the prospective development of the Register would enable the subset, mailmerge and analytical functions to be utilised to aid in patient management. A subset of patients could be generated of those who had failed to attend clinics for over two years or of those who had been lost to follow-up. A personalised letter could then be produced to either a patient or his or her GP suggesting further follow-up or asking for information regarding the patient's health or whereabouts. The inclusion of disease activity and morbidity scores prospectively would also permit crude but direct comparisons over a period of time or between different forms of treatment.

These observations suggest, therefore, that the existing computer system can be used as a basis for the implementation of a microcomputer based area Crohn's disease Register. The inclusion of data enquiry, analysis and mailmerge facilities has confirmed the system's value in audit and research, and alluded to its potential in patient management.

The features described have had far reaching implications for the computer system.

Clinicians who saw the system in operation felt that it contained many facilities which would be of value in their own clinical practice. This period coincided with a rapid increase in the number of microcomputers within the medical workplace, brought about mainly by a significant reduction in their cost. The purchase of machines mainly for word processing and data collection projects highlighted the scarcity of medically orientated database software packages. Although many good commercial database systems exist most require some knowledge of computers. Furthermore because most have been directed at the business user they have been developed primarily to

handle numerical information and are less supportive of non-numerical data. Although some medical data is numerical, a great deal is non-numerical (eg symptoms, treatment) and is therefore less suited to these commercial packages. This, in conjunction with the cost of the few commercially available medically orientated systems, suggested that there would be an ever increasing demand for a software package which incorporated many of the facilities included in the Crohn's disease Register system.

The demand in Tayside for this type of software grew so rapidly that it was decided to develop the facilities created for the Crohn's disease Register system into a general database management package. This would allow individual users to set up studies or applications around their own data sets. Once created they would then have access to all the existing data input, enquiry and analysis routines.

The package, which has become known as 'CRAFT' (Clinical Retrieval Analysis & Follow-up Template), contains programme modules for the generation of a database, data input and data management. Over the past 18 months ten different departments in the hospital have utilised CRAFT for one or more applications (discussed in the following chapter). At the time of writing most applications generated using the system have been set up to perform medical audit or have been used to help in research projects. More recently however further modules have been developed to enhance the patient management potential of the system. Two further more dedicated systems have therefore been created -CRAFTLIST - which is a waiting list system used to help in the management and audit of a department's or health board's surgical or outpatient waiting lists. The waiting list system contains a special module which has been dedicated to the operations required to arrange and manage a waiting list. It produces lists of patients, for example a week's admissions which can be sent to wards, medical and x-ray filing, and sends personalised letters to patients requiring admission. One such system runs the district Urology waiting list while a further system is presently being configured for the

district inpatient and outpatient Orthopaedic service. Parties both within and outwith our health authority are examining the potential of its more widespread use.

The second system - CRAFT-CLINIC - has been directed at specific hospital clinics and general practice. The initial aim was to provide a clinic or practice with a database which was appropriate to their needs. Each system is based on an age/sex register and has a number of 'clinics' or sections associated with it, for instance diabetics, geriatrics, well-woman, cardiovascular-risk screening, depending on the interest of the practice. Several practices have chosen this package to monitor and audit areas of their practice which are of particular interest. The system can easily be set up with any combination of 'clinics', most contain an age/sex register, and have one or a number of other 'clinics' such as diabetic, geriatric, paediatric, cardiovascular-risk screening and well woman. Indeed the list of available 'clinics' continues to expand. The CRAFT-CLINIC system has other added facilities directed specifically at data display, either on the screen or as hardcopy. It is particularly useful in the clinical situation where it permits the user rapidly to display information in a number of appropriate formats. Indeed these display options have led some hospital clinicians to look at the CLINIC system as an option to aid there specialised hospital clinics. This interest has resulted in the author obtaining support from a pharmaceutical company for the diabetic hospital clinic system, which is geared to diabetic shared care. The first of these systems was on site in early 1988.

It is suggested that the implementation of CRAFT systems into general practice should run alongside the well established GPASS system and be complimentary to it.

Summary

The value and implications resulting from the development of the initial computer system have been discussed. This has not only confirmed the value and potential of the system in the management of the Crohn's disease Register but has also

highlighted its more general potential in medical practice. The existing applications are briefly discussed in the next section.

6.6 APPLICATIONS USING THE CRAFT COMPUTER SYSTEM

Applications created using the present CRAFT system and the more recent CRAFT-LIST and CRAFT-CLINIC developments have been set up to help in one or a combination of medical audit, research and patient management.

6.6.1 Clinical Audit

The system is particularly valuable in this area because all data contained in a particular application can be audited in a variety of ways. Several disease registers have been generated apart from the initial Crohn's disease register. A Culposcopy clinic register will shortly be supplemented by the development of a Gynaecological Cancer Register for the area. A Bladder Cancer Register, one of the first applications to be set-up using the CRAFT system, at present contains data on all patients with bladder cancer in the area and contains information dating back as far as the late 1960's. These types of applications provide valuable epidemiological information on diseases within the area while the database can also act as a focal point for further specific research. This type of data is also valuable to the management team in measuring the size of a problem and hence resource requirements. For example in Tayside 3,420 cystoscopies have been performed on individuals with bladder tumour over the past 16 years. Trends can also be calculated from this data and projections made as to the future need for resources. Similarly the cost effectiveness of radiological investigation has been highlighted in the Crohn's study where it was found that the proportion of radiological investigations reported as normal in the Crohn's population has increased dramatically over the past few years, and confirms that the rate of positive return for the standard radiological investigations has decreased significantly (Table 5.29) over the years.

In 1986 the package was used to audit deliveries in the obstetric departments of Tayside and has been used to produce the annual returns to the health board and the

Scottish Office. CRAFT systems also operate in the Paediatric department where similar information is collected as required by the Scottish Office on neonates and over the perinatal period - the SMR11 official data collection form. Facilities have been developed to transfer data to other computer systems and with a little co-operation it would be possible to transfer this SMR11 information to the system in the Scottish Office either via modems or floppy disk. A similar local audit of the Special Care Baby Unit also uses the CRAFT system. A module has also been developed which utilises the SMR11 database to create and generate discharge letters on each baby leaving the neonatal paediatric unit.

For several years the psychiatric services in Tayside have logged patient contact data with a system based on the Health Authority's mainframe computer. For a number of reasons clinicians have been unable to readily retrieve information from this mainframe system. The imminent demise of this system has resulted in the Psychiatric service choosing the CRAFT system to continue this data collection. One main reason for this choice being the type of "hands on approach" which CRAFT has adopted and which enables clinicians to analyse data themselves as required. Three similar systems have therefore been created to manage each of the three health district's psychiatric contacts.

6.6.2 Research Work

Many of the applications created for basic audit can utilise CRAFT's flexible analysis facilities to facilitate further research on the collected data.

Several applications have been set up specifically as research projects, a gastric cancer trial sponsored by the MRC, a study into the effect of gut stimulant on post-op ileus and a project investigating various parameters in normal and abnormal pregnancies are all on-going projects which will begin to produce their results in a few months time. The department of Neurology has also recently begun a long term study to monitor and investigate the epileptic population of the area.

The department of Dermatology and Photobiology have also embarked on a long term data collection project which will act as a research and audit tool over many years.

Although many of these studies have been generated as research projects the databases created can also provide information on which to base further research. The ability to perform true adhoc enquiry and analysis gives great flexibility and power to the system which normally produces regular routine audit. This is only made possible by the rapid processing capability of the computer.

6.6.3 Patient management

Several of the recent systems have moved into the area of patient management and have resulted in the development of the CRAFT-LIST and CRAFT-CLINIC systems. This is however a different type of situation with the data being more dynamic in nature and where speed of operation is an important consideration with the secretarial staff using the system in real time as part of their routine work.

A Urology waiting list system has been created to oversee the waiting list and to perform basic monthly audits required by the health board. The system also generates admission and filing room lists each week as well as generating admission letters for patients. Ranked and ordered lists can be produced by age, date put on list, type of operation, consultant or indeed on any of the data contained within the system. A similar system is presently being set-up to oversee and manage Orthopaedic outpatient clinics and inpatient waiting lists.

A second and ambitious system has also be generated for General Practice. Many systems exist for use by General Practitioners and all have advantages and disadvantages. Those opting for the CRAFT-CLINIC system felt that the flexible and complex data manipulation facilities plus the potential for further development lent itself to their practices where audit and research were given some degree of priority. The

systems contain a combination of 'clinics' or sections; an age/sex register, cardiovascular-risk screening file, a diabetic recall monitoring section and well woman data which includes cervical smear data and recall, contraceptive data and breast examination information being a common combination. It is hoped that this will be a precursor to further GP orientated systems - indeed it is very easy to create further 'clinics' as appropriate to a particular practice. Finally endoscopy, breast and lithium clinic, intensive care and general surgical and vascular audit systems are all at varying stages of development.

Modular development of the system from a set of basic computing "tools" has enabled further modules to be created to perform specific tasks within a system with comparative ease - of particular relevance in patient management systems. The gastric cancer register has a "front end module" which registers and randomises patients before entry into the study. The success of the neonatal audit has resulted in the development of an "intelligent" discharge summary based on information contained within the neonatal database which generates discharge summaries in letter form for those discharged from the neonatal unit.

The computerisation of diabetic clinics has long been at the forefront of computer utilisation in the medical field - we have therefore developed specific facilities to help in the monitoring of this group of patients and have created a data set which will enable a shared care scheme to operate.

Commercial interest in the software has also resulted in a module being developed to enable the CRAFT system to be integrated with a commercially produced urodynamics system. This integration permits data produced within the urodynamic system to be downloaded into the CRAFT database where it can then be stored and manipulated with the package's facilities.

Although all applications discussed relate directly to medical data collection this need not be the case. At present one application has been created in the form of a

breast reference bibliography. Reference data is logged with the system which can then be searched by keywords, authors, journal etc and then summaries or abstracts from the bibliography printed out.

This short summary highlights the versatility of the CRAFT software. However it would be wrong to suggest that the system is the answer to all clinician's computerisation ideas. It merely demonstrates one pathway a clinician may take and one possible approach to software development in the medical field.

6.7 FUTURE DEVELOPMENTS

The development of CRAFT's facilities is an on-going process. Many of CRAFT's existing facilities continue to undergo further development. The impending introduction of mainframe Patient Administration Systems has also placed the development of a truly multi-user system and communication modules on CRAFT's critical pathway of development. The CRAFT project which initially required only my own time has grown and now involves all members of the Medical Computing Unit plus myself both to support existing users and continue further developments.

CHAPTER 7

CONCLUSIONS

The development and analysis of the Register has confirmed the clinical impression of a high incidence of Crohn's disease in Tayside region. Incidence and prevalence rates are higher than in some areas of the country but more interestingly are also at variance with those rates and trends from neighbouring Grampian region.

The retrospective audit and analysis of the Crohn's population has confirmed that much useful medical data can be gleaned from the Register. The value of the Register as a research tool has also been demonstrated; some of these findings require more detailed investigation. This illustrates the value of rapid data processing techniques and endorses the epidemiological approach as a means of identifying facts or associations which merit further investigation. No attempt has been made to use the Register in a prospective patient management role. However, the facilities incorporated in the computer system, which have subsequently been shown to be of proven value in other management type applications, confirm the potential for this role as the Register proceeds to the prospective phase of development.

The retrospective development of the Register has demonstrated that it is quite feasible to develop a disease register on a microcomputer system. It has been established that many facilities can be built into the system to firstly reduce the time required to manage the Register, and secondly to enable detailed and extensive ad-hoc enquiry of collected data. Although this development lends itself to the prospective implementation of the Register, both geographical and local practical difficulties place an obstacle in the path of immediate prospective implementation.

Although the present register relates to patients with Crohn's disease other chronic diseases such as diabetes and rheumatoid arthritis could similarly be monitored using this mechanism.

The demand for the computer system which has evolved from the Register's implementation and which has become known as CRAFT (Clinical Retrieval & Analysis Follow-up Template) has highlighted the need for a microcomputer based database management system directed specifically at the medical user. The implementation of applications in over ten departments within Tayside and others outside this region has shown the value of the 'hands on approach' to computerised data collection and has proved the system to be a valuable tool in aiding general medical audit, research and patient management. The recent development of the more dedicated 'CRAFTLIST' and 'CRAFTCLINIC' concepts shows that the continued growth of the system is assured at least in the short to medium term. The success of the computer package can be attributable firstly to the scarcity of commercially available medically orientated database management systems and secondly because the 'fourth generation techniques' used in its development permit the implementation of other applications with relative ease without recourse to further programming.

APPENDICES

DIAGNOSTIC SCORING SYSTEM FOR THE REGISTER

A. Scheme to determine IBD or otherwise

1. Symptoms

score 1 for each symptom related to possible IBD

Sub-total

2. Radiological criteria

no evidence IBD	=0	
some evidence IBD	=2	Sub-total
definite evidence IBD	=4	

3. Endoscopic criteria

no evidence IBD	=0	
some evidence IBD	=1	Sub-total
good evidence IBD	=2	

4. Pathological criteria

no evidence IBD	=0		
some evidence IBD	=1		
good evidence IBD	=3	Sub-total	
diagnostic Crohn's/UC	=5		**TOTAL**

SCORE 6 OR MORE WITH AT LEAST HALF OF ALL CROHN'S RELATED INVESTIGATIONS SHOWING A SCORE OF >0 THEN PATIENT HAS INFLAMMATORY BOWEL DISEASE.

Appendix 1a

B. Scoring system to determine Crohn's / Ulcerative colitis (Clinical section)

Clinical

1 Age	
<19	1
50-59	-1
>70	-2
2 Duration	
1-3mth	-2
3-6mth	-1
3 Family History	
U.C.	-2
Crohns	4
4 Patient history	
appendicitis	3
anal fissure	7
fistula	4
nil	-1
5 Site pain	
R lower	10
L lower	-1
R 1/2	2
L 1/2	-6
central	2
6 Type of pain	
severe	2
steady	2
7 Bowels	
normal	1
*1/day	3
*10/day	-2
8 Blood Pr	
nil	6
slight	-2
+ +	-5
9 Mucus	
nil	3
slight	-1
+ +	-2
10 Complications	
perianal	7
fistula	8
systemic	1
11 Nutrition	2
12 Tenderness	
R lower	10
upper 1/2	-2
L 1/2	-3
central	6
nil	-1
13 Abdo findings	
distend	2
mass	10

CLINICAL TOTAL

Scoring system to determine Crohn's / Ulcerative colitis
(Investigations section)

Investigations

1 Radiology	
normal	-3
continuous	-1
segmental	11

2 Site	
jejunum	7
ileum	31
R colon	1
L colon	-1
rectum	-3

3 Findings	
stenosis	4
ulcers	-1
dilatation	4
fistula	6
skip lesion	8

4 Endoscopy	
normal	12
ulcers	-3
stenosis	2
bleeding	-4
diffuse	-2
patchy	16

5 Biopsy	
normal	5
ulcers	-3
giant cell	20
granuloma	27
mucosal	-1
transmural	16

Lab tests	
Hb < 10	-1
WCC > 20000	1
Alb < 5gd/l	-1
Platelets	
> 400000	1
< 150000	-6
iron 20-40	1

INVESTIGATION TOTAL =

IF INVESTIGATION + CLINICAL SCORE > 10 THEN PATIENT CONSIDERED TO HAVE CROHN'S DISEASE

Appendix 1c

General Information

Full name
Address
Community Health Index identifier
Sex
Date of birth
GP name
GP address
Marital status
Religion
Occupation
Race
Social class
Birthplace
Area living when symptoms began
Type accommodation
History
    date onset
    symptoms and duration
    associated symptoms
    seasonal change
    aggravating factors
    affect of medication
Past medical history
Smoking
Alcohol
Breast fed as child
Number in family
    children specific GI disease
Family history
    type of disease
    who has disease
    relationship
    proximity
    degree contact

Appendix 2

Investigations

Radiological
- date
- type exam
- anatomical site
- findings
- diagnosis

Pathological
- date
- gross/biopsy specimen
- naked eye appearance
- anatomical site
- findings

Endoscopy
- date
- procedure
- distance scope to
- biopsy
- site
- general changes
- specific findings
- diagnosis

Haematology/Biochemistry
- date
- Hb
- WCC
- Platelets
- Viscosity
- C-reactive protein
- Urea
- Na
- Cl
- K
- blood sugar
- bilirubin
- alk phos
- GGTP
- albumin
- total protein
- transferrin
- B_{12}
- iron
- folate

Appendix 3

Treatment

Medical
- date
- type
  - none
  - symptomatic
  - anti-inflammatory
  - dietary
  - miscellaneous

Surgical
- date
- type
- indications
- operation included

Morbidity

frequency of symptoms
restriction to normal life
who educated patient about disease
lost work
knowledge of Crohn's disease
sleep loss
mental health suffered
memebers IBD association
productive life
affect of menstrual cycle

Appendix 4

Appendix 5 which follows in the following pages is an example of the questionnaire used in the initial case capture of the retrospective data.

Appendix 5

CROHNS REGISTER ENTRY FORM

SURNAME
FORENAME
MPI
ADDRESS

GP NAME
GP ADDRESS

DIAGNOSTIC SCORING SYSTEM

IS THIS IBD OR NOT

CLINICAL	ENDOSCOPIC	RADIOLOGICAL	PATHOLOGY
SCORE 1 FOR EACH +VE	NO EVIDENCE OF IBD =0	NO EVIDENCE OF IBD =0	NO EVIDENCE OF IBD =0
SYMPTOM DIRECTLY RELATED	SOME EVIDENCE OF IBD =1	SOME EVIDENCE OF IBD =2	SOME EVIDENCE IBD =1
TO POSSIBLE IBD	GOOD EVIDENCE OF IBD =2	DEFINITIVE EVIDENCE IBD=4	GOOD EVIDENCE OF IBD =3
SCORE=	SCORE=	SCORE=	DIAGNOSTIC FOR CROHNS/UC=5
			SCORE=

TOTAL SCORE

If the total score is >=6 and at least two of the above questions have a score 0 then consider the patient to have IBD.

IF THE ABOVE SCORE >6 THEN IS THIS CROHNS OR ULCERATIVE COLITIS

CLINICAL

A AGE:
- <19 =+1
- 50-59 =-1
- >70 =-2

B DURATION:
- 1-3MTH =-2
- 3-6MTH =-1

C FAMILY HISTORY:
- UC =-2
- CROHNS =+4

D PATIENT HISTORY:
- APPENDICITIS =+3
- ANAL FISSURE =+7
- FISTULA =+4
- NIL =-1

E SITE OF PAIN:
- RT LOWER QUAD =+10
- LT LOWER QUAD =-1
- RT 1/2 =+2
- LT 1/2 =-6
- CENTRAL =+2
- NIL =-1

F TYPE OF PAIN:
- SEVERE =+2
- STEADY =+2

G BOWELS:
- NORMAL =+1
- +1 DAILY =+3
- +10 DAILY =-2

INVESTIGATIONS

H BLOOD PR:
- NIL =+6
- SLIGHT =-2
- ++ =-5

I MUCUS PR:
- NIL =+3
- SLIGHT =-1
- ++ =-2

J COMPLICATIONS:
- PERIANAL =+7
- FISTULA =+8
- SYSTEMIC =+1

K NUTRITION:
- EMACIATED =+2

L TENDERNESS:
- RT LOWER QUAD =+10
- UPPER 1/2 =-2
- LT 1/2 =-3
- CENTRAL =+2
- NIL =-1

M ABDO FINDINGS
- DISTENSION =+2
- MASS =+10

N RADIOLOGY:
- NORMAL =+3
- CONTINUOUS =-1
- SEGMENTAL =+11

O SITE:
- JEJUNUM =+7
- ILEUM =+31
- RT COLON =+1
- LT COLON =-1
- RECTUM =-3

P FINDINGS:
- STENOSIS =+4
- ULCERS =-1
- DILATATION =+4
- FISTULA =+6
- SKIP LESIONS =+8

Q ENDOSCOPY:
- NORMAL =+12
- ULCERS =-1
- STENOSIS =+2
- BLEEDING =-4
- DIFFUSE =-2
- PATCHY =+16

R BIOPSY:
- NORMAL =+12
- ULCERS =-3
- GIANT CELL =+20
- GRANULOMA =+27
- MUCOSAL =-1
- TRANSMURAL =+16

S LAB TEST
- HB<10 =-1
- WCC>20000 =+1
- PLAT<150 =-6
- PLAT>400 =+1
- IRON 20-40 =+1

TOTAL SCORE=
IF SCORE>10 THEN THIS IS CROHNS DISEASE

GENERAL INFORMATION

MARITAL STATE
1.single
2.married
3.widow(er)
4.separated
5.separated

RELIGION
1.protestant
2.catholic
3.jewish
4.other
5.not known
6.none

OCCUPATION
1.preschool
2.school
3.student
4.unskill.manual
5.skill.manual
6.clerical
7.farmer
8.white collar
9.managerial
10.profesional
11.homemaker
12.other

RACE
1.caucasian
2.negro
3.oriental
4.mixed
5.other

SOCIAL CLASS
1 2 3 4 5

BIRTHPLACE
1.UK 2.Other
name:

AREA LIVING WHEN SYMPTOMS BEGAN
1.UK or 2.other if UK postcode ie DD3
and
3.rural or 4.urban DURATION LIVED IN THIS HOUSE

INTENSITY OF POPULATION
1.live on own A.<aver population in house
2.live in family unit B.aver popultion in house
3.communal dwelling C.>aver population in house

HISTORY

Date onset

SYMPTOMS AND TIME IN MONTHS
1.diarrhoea
2.abdo pain
3.rectalbleed
4.fever
5.lassitide
6.wt.loss
7.fistula
8.anal lesions
9.other

ASSOC. SYMPTOMS
1.arthropathy
2.eye conditions
3.liver disease
4.skin problems
5.other

SEASONAL CHANGE
(W)orse (B)etter (U)nchanged
summer winter
autumn spring

INFLUENCE OF DRUGS ON SYMPTOMS
(h)elp (u)nchanged
(w)orsen (n)ot applic
antidiorrheal
antibiotics
the pill
steroids
metronidazole
salazopyrin
other
name:

AGGRAVATING FACTORS
a.enteric infect h.none
b.other infect i.URTI
c.diet indescrtion j.Ba enema
d.pregnancy k.surgery
e.physical stress l.fatigue
f.emotional stress m.menses
g.alcohol n.other

PAST MEDICAL HISTORY

a.none
b.GI
A peptic ulcer B haemorrhage C anaemia
D perforation E stricture F fistula
G fissure H ileus I obstruction
J enteritis K pericolitis L peritonitis
M stomatiotis N polyps O malignancy
P pancreatitis Q gallstones R varices
S liver dis. T jaundice U coeliac dis
V nutrit.defic W other I growth retard
c.eye
A iritis B other
d.Neuropsychiatric
A psychosis B neurosis C other
f.Dermatology
A pyoderm gan B erythema nodosum
C other D abscess

f.Cardiovascular
A Rh fever B myocarditis C endocarditis
D phlebitis E IHD F CVA
G hypertension H other I PVD
J DVT
g.Genito/urinary
A UTI B nephrolith. C period irreg.
D subfertility E other
h.Musculoskeletal
A arthralgia B arthritis C spondylitis
D osteoporosis E sacroileitis F other
i. Respiratory tract
A TB B sarcoid C asthma
fibrosing alveolitis
j.Miscelan.
A diabetis B drug reaction C collagen dis.
D amyloid dis. E allergy

Smokes
1.never
2.yes cigs nos day
tabacco oz/week
3.previously how long
when stopped

Alcohol intake
never/min/mod/heavy
in units per week

BREAST FED AS A CHILD Yes/No

NOS. OF CHILDREN IN FAMILY
ANY CHILDREN HAD GI DISEASE
Name the disease:

FAMILY HISTORY

Type of Disease
A UC B Crohns
C carcinoma D peptic ulcer
E biliary disease F liver disease
G allergic disease H collagen disease
I arthropathies J psychiatric disease
K other GI disease L other

Who has the Disease
A mother B father
C twin D brother
E sister F son
G daughter H grandp.mat
I grandp. pat J aunt/uncle
K neice/nephew L other

Relationship
1 natural
2 by marraige
3 by adoption

Proximity
1 now in same house
2 prev.in same house
3 within 50 miles
4 > 50 miles

Degree of contact
at present and in the past
1 often 4 often
2 seldom 5 seldom
3 never 6 never

TYPE	WHO HAS	RELATION.	PROXIMITY	CONTACT

INVESTIGATIONS 1

HAEMATOLOGICAL

TYPE	DATE	VALUE	TYPE	DATE	VALUE
HB			BILIRUBIN		
WCC			ALK PHOS		
PLATELETS			GGTP		
VISCOSITY					
C-REACTIVE PROTEIN			ALBUMIN		
			TOTAL PROTEIN		
UREA			TRANSFERRIN		
NA					
CL					
K					
BLOOD SUGAR					

ENDOSCOPY

FILL IN THE TABLE BELOW WITH THE APPROPRIATE NUMBERS TO REPRESENT FINDINGS

ANATOMICAL SITES	PROCEDURE	TYPE OF CHANGES	FINDINGS	
A oesophogus	A gastroscopy	A normal	A oedema	I atrophy
B stomach	2 ERCP	2 acute	B erythema	J narrow lumen
C pylorus	3 colonoscopy	3 chronic	C spontan. bleeding	K polyps
D duodenum	4 sigmoidoscopy	4 acute & chronic	D pus	L malignancy
E jejunum	5 proctoscopy	5 tumour	E ulcer	M diverticulum
F ileum		no information	F multiple ulcers	N stricture
G caecum			G friable mucosa	O normal
H asc. colon			H pseudomembrane	
I transverse colon				
J sigmoid colon				
K rectum				
L anal canal				

DATE	PROCEDURE	SCOPE TO ANATOM SITE	BIOPSY Y/N	GENERAL CHANGES TYPE	GRADE	SPECIFIC FINDINGS SITE	FINDINGS

THE CHANGES ON COLONOSCOPY/SIGMOIDOSCOPY/PROCTOSCOPY SUGGESTED A DIAGNOSIS OF

1 UC	5 Diverticular disease
2 Crohns	6 pseudomembranous colitis
3 Non specific colitis	7 No abnormality
4 Tumour	

A DEFINITIVE DIAGNOSIS was known / was suspected / was not suspected BEFORE THIS INVESTIGATION.

INVESTIGATIONS 2

RADIOLOGY

Fill in the table with the appropriate letters/numbers

ANATOMICAL SITE

A oesophogus
B stomach
C duodenum
D jejunum
E ileum
F terminal ileum
G small bowel
H appendix
I caecum
J asc colon
K trans. colon
L desc. colon
M sigmoid colon
N whole colon
O rectum
P anal canal
Q skin
R bladder
S pancreas
T vagina
U gallbladder
V kidney
W ureter
X CBD
Y gallbladder

TYPE OF EXAM

A plain abdo
B Ba meal
C Ba meal & FT
D Ba enema
E small bowel enema
F oral cholecyst.
G IVC
H Ultrasound
I IVP
J fistulogram
K CAT scan
L isotope scan
gallium/lab wc/indium
other

DIAGNOSIS

A normal
B no signif abnorm.
C inflam disease ?type
D Crohns disease
E ileo-colitis
F Ulcerative colitis
G non specific proctitis
H peptic ulcer disease
I cholilithiasis
J renal calculi
K obstructive uropathy
L abscess
M other

FINDINS

1 possible
2 definite
3 benign
4 malignant
5 partial
6 complete
7 single
8 multiple
use the above to help decribe those below

A narrowing
B obstruction
C fluid levels
D dilatation
E perforation
F diverticuli
G abdo mass
H reduced function
I calculi
J cavity
K fistula
L polyps
M shallow ulcers
N deep ulcers
O longtitudinal ulcers
P transverse fissures
Q stricture
R sinus tract
S skip areas
T thickened walls
U cobblestone pattern
V abscess
W pseudopolyps

DATE	TYPE EXAM	DIAGNOSIS	FINDINGS

PATHOLOGY

Fill in the table with the appropriate letters/numbers

ANATOMICAL SITE

A oropharynnx
B oesophogus
C stomach
D duodenum
E jejunum
F ileum
G caecum
H asc. colon
I trans. colon
J desc. colon
K sigmoid colon
L rectum
M anal canal
N liver
O skin
P other

GROSS / NAKED EYE APPEARANCE

A one area
B > one area
C skip lesions
D thickened bowel wall
E thickened submucosa
F ulcerated mucosa
G fistula to the skin
H fistula to other organs
I mesentery thickened
J regional lymphadenopathy
K stricture
L serosal injection
M signs of proximal obstruction
N other

MICROSCOPIC APPEARANCE

A acute inflam exudate
B non specific infiltration withchronic inflam cells
C mainly plasma cells,macrophages,eosinophils
D fibrosis
E giant cells
F granulomatous lesions
G reactive hyperplasia in the lymph nodes
H goblet cell depletion
I crypt absces
J presence of paneth cells

DATE	SPECIMEN GROSS/BIOPSY	GROSS APPEARANCE SITE	GROSS APPEARANCE FINDINGS	MICROSCOPIC APPEARANCE SITE	MICROSCOPIC APPEARANCE FINDINGS

EXTENT OF DISEASE
1 small bowel
2 ileo colic
3 large intestine
4 discontinuous disease

MORBIDITY

Symptoms cause trouble

1.daily
2.few times a week
3.several
4.every few months
5.seldom
6.never

Symptoms restrict normal life

1.lost a job
2.caused a change in job
3.restrict sport/hobbies
4.affect social life
5.affect sex life
6.reluctance to plan future activities

Where do you learn about your disease

1.hospital doctor
2.GP
3.nurse
4.magazine
5.books
6.friends
7.none of the above

Have lost work

1.every month
2.every 3 months
3.every year

How much do you know about your disease

1.none 3.wish to know more
2.little 4. lot

SYMPTOMS HAVE CAUSED LOSS OF SLEEP YES/NO
HAS MENTAL HEALTH SUFFERED YES/NO
ARE YOU A MEMBER OF THE CROHNS/COLOSTOMY/ILEOSTOMY ASSOC. YES/NO
WOULD YOU JOIN ANY OF THE ABOVE ASSOCIATIONS YES/NO
DO YOU FEEL YOU LEAD A FULL PRODUCTIVE LIFE DESPITE YOUR DISEASE YES/NO
DOES YOUR DISEASE AFFECT YOUR MENSTRUAL CYCLE WORSE/NO CHANGE/BETTER
DOES YOUR PERIOD AFFECT YOUR SYMPTOMS WORSE/NO CHANGE/BETTER

DISEASE ACTIVITY INDEX

NOS LIQUID STOOLS IN ONE WEEK
SCORE
none =0
1-4 =1
5-9 =2
10-19 =3 SCORE
20-49 =4
50-99 =5

SUM OF SEVEN DAILY ABDO PAIN READINGS
none=0 mild=1 mod=2 severe=3
SCORE=

GENERAL WELL BEING SUM OF 7 READINGS
well=0 (par=1 poor=2 very poor=3
terrible=4
SCORE=

SYMPTOMS RELATED TO CROHNS
A arthritis B skin/mouth lesions
C iritis/uveitis D perirectal problems
E febrile episode in past week
F presence of fistula
score 1 for each SCORE=

ABDO MASS
no mass=0
? mass =2
mass =5
SCORE=

BODY WT
% below norm wt.
SCORE=

TREATMENT date

MEDICAL

A None

SYMPTOMATIC
B antidiorrhoeal
C laxative
D analgesia
E psychotherapy

ANTI-INFLAM/IMMUNOSUPPRES.
F steroids
G salazopyrine
H azothiaprine

A small bowel resection
DIETARY
I diet
J elemental diet
K TPN
L vitamins
M other:
H localised resection
MISCELANEOUS
N antibiotics
O metronidazole
P iron prep

SURGICAL

INDICATIONS
A obstruction
B stricture
C fistula
D abdo mass
E abscess
F perforation

G peritonitis
H failed medical Rx
I uncertain diagnosis
J cholelithiasis
K growth retardation
L other

OPERATION
date
type
INCLUDED:

B large bowel resection
end to end anastomosis
D side to side anastomosis
E one area resected
F 2 areas resected
G 3+ areas resected

I radical resection
J drainage of abscess
K ileostomy/colostomy
L bypass operation
M stricturoplasty
N other

Prospective Mailing Questionnaire

Crohns Register office
Dept of Surgery
Ninewells Hospital
Dundee
Date

Dear **Name,**

It is now nine months since we were last in contact with you regarding your Crohn's disease - we hope you are well.

We would again be grateful if you would fill in the enclosed questionnaire on the progress of your disease. This information will enable us to further understand this disease and hence improve our methods of treatment.

If you wish any further information on your disease please contact us directly or ask your doctor to contact us and we will send him the information directly.

Yours Sincerely,

Please answer the following:-
Since we were last in touch have you

a. seen your GP about your Crohn's disease
b. seen a hospital doctor about your Crohn's disease
c. been admitted to hospital with your Crohn's disease

if yes

i. which hospital
ii. when was it
iii. can you name investigations
iv. did you have an operation

Appendix 6a

Present History

1.Symptoms

diarrhoea	}
abdo pain	}
lassitude	}daily/each week/monthly
weight loss	}
bleeding back passage	}

associated symptoms
joint / eye / skin / other problems

2.Seasonal pattern
symptoms have been worse in
summer / autumn / winter / spring

3.Have any of the below made symptoms worse (circle as reqd)

nothing apparent	any type infection
diet indiscretion	other investigations
surgery	pregnancy
physical stress	tiredness
emotional stress	periods
alcohol	

4.Present medication
anti-diarrhoeal
falgyl/metronidazole
salazopyrine
steroids
antibiotics
other (please name)

Disease activity score for past week

1. Nos of liquid stools per week
0 / 1-4 / 5-9 / 10-19 / 20-49 / 50-99
(please circle as required)

2. Sum of seven daily abdo pain readings
none / mild / moderate / severe

3. General well being - sum of seven daily measurements
well / slighly below par / poor / very poor / terrible

4. Symptoms related to Crohn's in past week
joint / skin /mouth / eye problems / anal irritations /
episodes of fever

5. Weight

Appendix 6b

MORBIDITY QUESTIONNAIRE
HOW DOES THE DISEASE AFFECT YOUR DAILY LIFE

1. Symptoms cause trouble
   daily / few times week / several times month / every few months / seldom / never

2. Over past 9 months my symptoms have caused
   loss of job / change in job / restricted sports hobbies affect social life / affect sex life / reluctant to plan future activities

3. Symptoms have caused loss of sleep

4. Have you lost work
   every month / every 3 months / once a year

5. Has mental health suffered because of your disease

6. How much do you know about your disease
   none / little / a lot / wish to know more

7. Do you lead a full productive life despite your disease

8. For women
   a.Does yor menstrual cycle affect your symptoms worse / same / better

   b.Does your disease affect your menstrual cycle worse / same / better

Appendix 6c

Publications

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